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URÆMIA IN BRIGHT'S DISEASE.

URÆMIA
IN BRIGHT'S DISEASE:

ITS CLINICAL MANIFESTATIONS, PATHOLOGY AND TREATMENT.

BY

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URÆMIA IN BRIGHT'S DISEASE.

URÆMIA is the name which was given by Piorry to the condition about to be described, and although it suggests a pathology which modern investigation does not support, it has received a general acceptation, its real significance being now neglected. It is derived from *οὖρον* urine, and *αἷμα* blood.

DEFINITION.

Uræmia is a clinical term applied to a group of nervous symptoms occasionally met with in certain pathological conditions, in which there is either partial, or complete failure of the renal function.

CAUSATION.

This failure on the part of the kidneys is, by the majority of investigators, now regarded as a failure in their excretory functions; but there are some who maintain, that the fault lies in the inability of the diseased organs to elaborate a secretion, which, in health, passes into the system, and is of service to the whole economy.

Uræmia is not an uncommon complication in the following diseased states :—

(1,) Any of the different forms of Bright's disease.

(2,) Cystic, tubercular, and cancerous kidney diseases.

(3,) Suppurative nephritis.

(4,) Any condition in which there is either obstructive, or non-obstructive anuria.

The existence of any of the above pathological states, by no means necessitates an early uræmic attack.

The onset of uræmia, in even the most severe forms of kidney mischief, is frequently delayed many days or even weeks. Biermer's case of a patient who lived 118 days without showing uræmic symptoms, although there was complete anuria during the whole of this time, somewhat taxes the credulity, and is certainly a record. There are, however, other instances well authenticated, in which uræmia did not occur, although anuria was complete, and lasted three or four weeks.

On the other hand, uræmia sometimes supervenes when kidney mischief is slight, and it then appears out of proportion to its cause. Uræmic symptoms may, however, generally be expected on the second or third day, dating from the establishment of complete anuria.

Anuria does not furnish anything but a minority of the uræmia which is met with in medicine. It is, in connection with pregnancy associated with kidney disease, granular contracting kidney, and scarlatinal nephritis, that the great majority of cases arise. Incompetence on the part of the kidney to excrete the excrementitious substances, in part or in whole, must always be regarded as a state in which uræmic symptoms may be expected. As the healthy kidney is an organ in whose function there is great latitude, incompetence becomes nearly a relative term. Elimination of the waste products of the body, may be, for any length of time, satisfactorily carried on by kidneys moderately diseased, provided no undue stress is thrown upon them, they are then, for the organism, and under these circumstances, physiologically competent; elimination during

twenty-four hours, is equal to the formation of the waste products of the body occurring in that period ; no toxic material accumulates, no uræmia results. Suppose an increased effort is demanded of these organs ; suppose the formation of toxic material is increased ; or, suppose a temporary diminution in the function of the remaining healthy tubules, which up to now have efficiently carried on more than their normal work, a break-down of the whole excretory apparatus not uncommonly results ; the elimination becomes defective, and the organism is poisoned. Thus, renal structures competent under certain circumstances, become incompetent under others, and so no amount of pathological change in the kidneys is necessarily related to a fixed amount of functional incompetence, when the other existing circumstances are unknown. Instances in which apparently normal kidneys proved themselves unable to deal with a large, and sudden addition to the normal waste of the body, resulting from violent, and prolonged exertion, are well known. A good example of an auto-intoxication by the products of metabolism, brought about in this manner, is frequently now seen in the headache, insomnia, and general lassitude, which commonly follows excessive exercise, such as bicycling.

The identification of the substance or substances present in the urine, which, being retained, give rise to toxic symptoms, has always proved a matter of much difficulty ; much labour has been expended upon the enquiry, and the most conflicting opinions have been derived from the results of many carefully carried out investigations and experiments.

Only the more important theories, which have been

advanced as an explanation of the pathology of the condition, will now be briefly reviewed ; and a re-statement made of the arguments advanced in support of each, and the objections thereto considered.

The theories, so far put forward, may be divided into three classes : the Mechanical; the Mechanico toxic; and the Chemical.

MECHANICAL THEORIES.—Owen Rees, Traube, and Rilliet, were the chief exponents of what is known as the mechanical theory of uræmia. It is to Traube, however, that it owes its elaboration, and it has received his name.

TRAUBE'S THEORY.—Traube assumed that, when uræmia occurs, the following conditions are always present :—

(1,) Hypalbuminosis of the blood.

(2,) Increased arterial tension.

(3,) Œdema and anæmia of the brain, resulting from the preceding states.

That hypalbuminosis frequently co-exists with uræmia is undoubted. The normal density of blood serum being taken as 1028, Bartels has observed it fall to 1015 or 1018; Christison, 1019; but even 1013 has been recorded.

In uræmia occurring in granular contracted kidney, Christison says the water of the blood is increased from 784 per 1000 to 821, whilst the albumen is reduced from 7·34 per cent. to 6·85 per cent.

Arterial tension is very commonly raised, in the uræmia which supervenes in the course of many kidney complaints ; and, notably, in uncomplicated cases of granular contracted kidney.

Traube went so far as to assert, that he never knew a case of uræmia, in which there was no co-existing ventricular hypertrophy of the heart. The hydræmic plethora and increased blood pressure, he considered sufficient to produce serous exudation from the capillaries, recognisable as œdema, or dropsy, diffuse or localised, according to the circumstances determining the one or the other. Uræmia would be the clinical feature, when this exudation occurred with sufficient severity to produce anæmia in the brain.

Coindet, and Odier, suggested that anæmia of the encephalon, is the result of the pressure exerted by the bony surroundings of the latter upon their contents, enlarged by the interstitial or ventricular dropsy present.

Traube even went so far as to localise the œdema, and anæmia of the brain, from the symptoms which an attack of uræmia presents.

Unconsciousness and coma, he said, indicate implication of the cerebral hemispheres. Convulsions, without coma, signify implication of the middle brain. Coma and convulsions, imply œdema and anæmia of both hemispheres and central portions.

Niemeyer says, that whatever may be found to be the ultimate cause of uræmic symptoms, œdema of the brain may be inferred :—

(1,) When the seizure takes the form of deep coma, with intermittent eclampsic spasms.

(2,) When, at the time of its occurrence, the secretion of urine is normal in quantity, or increased.

(3,) When there is marked œdema of the face.

(4,) When there is strong pulsation of the carotids.

The following experiment was devised and carried out,

with a view of demonstrating that œdema of the brain is sufficient to bring about symptoms resembling uræmia.

The ureters of a dog, having been first ligatured, the jugular veins were treated in like manner. Water was then injected into the carotids, and, the not very astonishing result, general convulsions, ensued. The autopsy shewed mere œdema of the brain, no hæmorrhage had taken place.

Falck also produced convulsions, and death, by injecting a quantity of water, equal to one fifth of the weight of a dog, into its veins.

It is difficult to attach much value to the conclusions drawn from such experiments. Both are what Bouchard would call "monstrous operations," which are not at all comparable to pathological states. It is quite impossible to compare this excessive hydræmia, to any like condition in disease, for in no disease does such a dilution of the blood take place.

Traube's theory has been attacked from all sides, and in whatever quarter it has been assailed, it has shewn fatal weakness.

Granting that hypalbuminosis of the blood is more or less pronounced in the majority of cases of uræmia, it has yet to be shown that œdema results from this condition. So far, legitimate experimentation has not lent any countenance to such an assumption.

Cohnheim, and Lichtheim, found, on the contrary, that an artificial hydræmia produced by the injection of large quantities of water, or neutral solutions, into the vessels of dogs, and other animals, does not give rise to dropsy of the limbs, nor skin, and certainly not to œdema of the brain.

The conclusion to be drawn from their experiments, and those of others, is that the capillary wall does not act like a dead membrane, it does not allow any excess of fluid to drain away into the tissues of an animal, unless, as Cohnheim proved, there is co-existent weakness of the vessel walls.

Richardson performed an heroic experiment, with the object of proving that œdema does not result from simple hydræmia. He injected a colossal quantity of water into the peritoneum of the dog, convulsions did not ensue, nor was œdema of the brain noticeable at the autopsy.

Bouchard shewed that when the density of the serum is reduced artificially to 1007, which he says is equivalent to an injection of 122 grammes of water per kilogramme of animal, then death results. When the amount injected equals 90 grammes per kilogramme of animal, signs of the disastrous effects it produces commence to appear.

Now, in the uræmia, which is met with clinically, it is exceedingly rare to find the density of the serum amounting to only 1016, 1013 being the lowest that has been recorded. Certainly no such figure as 1007 for the mean density of the blood serum was ever met with in any case of clinical uræmia, and this is the density at which Bouchard has conclusively proved that death occurs from simple dilution of the blood.

Furthermore, in some cases of complete anuria death takes place from uræmia, soon after the commencement of the second day. Now, if the secretion of urinary water during this time be taking place at the same rate as in health, and supposing that none of this fluid be

lost by vomiting, or diarrhœa, etc., as it frequently is, then the total quantity retained to the hour of death would not amount to 35 grammes per kilogramme of the individual; but, as just stated, it is necessary to inject a quantity of water, equal to 90 grammes per kilogramme of animal, before any injurious results become evident.

Dr. Carter, in the Bradshawe Lecture of 1888, supplied a powerful weapon to the opponents of Traube's theory. He proved that whatever may be the condition of the blood in patients dying with uræmic symptoms, œdema of the brain, at any rate, does not exist as a *post-mortem* fact, and so is probably not present in the previous uræmic state. His examinations were carried out with scrupulous care and exactitude. In the first place he observed the relative, and quantitative, amount of fluid existing in a normal brain. This he found to be 80 per cent. of the whole weight, the remaining 20 per cent. being solid residue. Treating, in the same manner, the brain of a patient who had died from scarlatinal nephritis with uræmic symptoms, he did not notice an increase in the amount of fluid present, but rather the reverse. In this case it constituted only 79·25 per cent. of the whole. In a second case the figures were 74·25 per cent. fluid, and 25·75 per cent. solid. This latter result seems to prove rather too much, but, it is to be remembered, that some vascular spasm may have existed throughout the brain prior to death, such as is commonly met with in other parts of the body in uræmia, Dieulafoy's "dead white hand" being a good example. Unfortunately, the absence of œdema can be accounted for, by supposing that the fluid has

drained away into the lymphatics, and so into the ventricles, thus escaping before the investigation commenced.

With regard to Traube's second assumption it is now generally recognised that high arterial tension is not always present in uræmia, and, therefore, cannot be regarded as an essential factor in the causation of the symptoms.

Bartels has reported several cases of uræmia, in which he noticed absence of cerebral œdema, hypertrophy of the heart, and also any diminution of the density of the serum.

Rommelaere, in explaining away the results of experiments which seemed to countenance Traube's views, agrees with Bidder, who thinks that the convulsions and coma observed after the injection of large quantities of water into the vessels of animals, are not the result of the dilution, but rather are caused by the increased blood pressure consequent upon the experiment; increased blood pressure, we have just seen, is not always present in uræmia, so that the theory does not receive even this support.

Traube's theory has obtained so much attention, and has for so long been looked upon as the true explanation of uræmia, that it now seems extraordinary that it should have successfully held the field for a day upon so slender a basis. All its supports have, however, at last been broken down, and the pile of evidence which has been collected, disproving it, is so great, that its resurrection under any guise would be remarkable. Nevertheless, in this theory, there is much that is in accordance with the more recent views of the etiology of convulsive

attacks; for example:—the researches of Küssmaul, and Tenner, have experimentally proved the dependence of convulsions on cerebral anæmia, and also those of Brown-Séquard have clearly shewn that an anæmic condition of the nerve centres, is the prelude of an epileptic attack.

Lichtenstein suggested what he considered an improvement of the theory. He asserted, that in uræmia, there is always inflammatory œdema of the brain substance, and meninges. The assertion, however, is directly contrary to fact, and may be dismissed at once. Popoff's theory is not very intelligible in the form he has put it. He imagines, that uræmia depends upon "the accumulation and change of the blood corpuscles in the capillaries of the brain," which seems to suggest a condition resembling that described by Lichtenstein, as a cause of the symptoms. It may therefore be dismissed as summarily.

THE MECHANICO-TOXIC THEORY.—Rosenstein is the apostle of the mixed, or Mechanico-toxic theory of uræmia, which pretends to be a compromise between the Mechanical, and Chemical theories. It is supposed to solve the difficulties of each, and to contain all their acceptable features.

Rosenstein believes that the primary change which takes place, is a spasm of the cerebral vessels, soon followed by exudation, œdema, and effusion into the ventricles. Should death occur during the initial stage, then no physical sign of the change is found at the autopsy. On the other hand, death later, would give an opportunity of detecting œdema of the brain, etc. In this manner, he attempts to satisfy both those who

assert that uræmia depends upon œdema, and those who contradict the statement.

Closer examination of the theory, shows that it really rests upon a chemical basis. The initial spasm which is followed by the other changes described, must be produced by some chemical agent, capable of so stimulating the vaso-motor centre, that the primary contraction results. Rosenstein's theory, then, is merely the explanation of the action of a chemical substance, and a detailed account of its secondary effects. Until Rosenstein has identified the substance, which is capable of effecting the initial contraction of the vessels, it seems rather premature to dogmatise upon its more remote action. His theory, therefore, depends upon the feasibility of the chemical theory, to which consideration will now be directed.

CHEMICAL THEORIES.—The theory, which suggests that uræmia results from the retention of some, or any, of the solids of the urine, is one of the oldest put forward to explain its genesis. The earlier investigators strove to find a single component of the urine; which, accumulating in the body, could bring about the various manifestations of uræmia. At the present time this attempt has been almost abandoned, a wider view of the causation of uræmic symptoms being now taken. They are becoming recognised as the result of a compound poisoning, by all the elements of the urine, many of which are physiologically antagonistic in their actions. The ever varying aspects of uræmia, are regarded now, as the clinical correlative of the total toxic action of an injurious product, composed of numerous simpler bodies, present in constantly changing proportions. There are,

however, some who still attribute uræmia to the effects of an exclusive action of a single poison, and still pin their faith on one or other of the older theories.

WILSON'S THEORY.—The opinion that uræmia arises from a defective elimination of urea, leading to its accumulation within the system, is one of the oldest of the chemical theories. Although it has been demonstrated that urea is not a powerful toxic substance, attempts are constantly being made to revive the theory in other forms, in which, to urea is no longer attached its pristine importance, but in which it figures merely as a co-operating factor of some consequence.

In health, the amount of urea excreted on ordinary diet, by a man of 66 kilogrammes, M. Foster gives as 33·180 grammes, or roughly ·5 grammes per kilogramme of body weight. There is a good deal of latitude in the quantity formed daily in quite normal conditions, and in like manner the urea found in the blood "varies from ·2 grammes to ·4 grammes per 1,000." (Payne.)

In certain forms of Bright's disease, the amount of urea excreted in the urine is much diminished, and may be only ·2 grammes per kilogramme in twenty-four hours. This reduction is found to be relatively greater than the reduction which takes place in the other urinary solids. But in patients suffering from lithæmic nephritis, there is no great diminution in the quantity of urea excreted. Bartels, and Grainger Stewart even assert that in these cases it is undiminished or may be increased.

In uræmia, an accumulation of urea in the tissues may frequently be chemically demonstrated. Bouchard says, that the blood of uræmic patients sometimes contains as

much as thirty-two times the normal quantity. In the muscles in health, only traces of urea can be found, but, in uræmia ·2 grammes have been detected.

Lionel Beale is inclined to regard these great increases, which are occasionally present, as entirely exceptional, and he accounts for them, by supposing that urine may have passed directly into the blood, by the rupture of the upper part of some of the uriniferous tubules; urine would then escape into a neighbouring capillary, or into the lymphatic system. On the other hand, those cases in which there is no increase of urea in the blood, he says may be due to the liver having ceased to act.

The vital question for Wilson's theory is, whether the amount of urea accumulated within the body in uræmia, is present in such a quantity as to act as an efficient poison, or no. That urea is toxic in huge doses, especially in those cases in which its elimination is retarded, is admitted by everyone. Voit says, any inert substance, foreign to the organism, and accumulating within the system, if present in sufficient quantity, will cause symptoms resembling uræmia. He observed that dogs fed upon food containing urea, and at the same time being permitted but little fluid to drink, soon show signs of uræmic poisoning; but, if the amount of drinking water be unlimited, then the addition of urea to the diet does not produce any injurious effects.

Meissener, and Hammond, found that death, preceded by convulsions, follows an injection of urea into the veins of nephrectomised dogs. It is important to note, that the convulsions produced by the injection were not intermittent.

In uræmia the body sometimes seems to be saturated

with urea, which is found in the vomit, in all the secretions (saliva, milk, etc.), and in the form of a glistening powder upon the skin of the body. It is also present in any exudation into the serous cavities which may have occurred. *A priori*, then, there would seem to be considerable reason to agree with Wilson's theory. There is, however, a great deal to be said against it.

Frerichs, and Oppler, repeated Micissener's and Hammond's experiments, and obtained only negative results. The cause of the discrepancy was shown, by Feltz and Ritter, to lie in the quality of the urea used. If urea containing ammonium carbonate, etc., as impurities, be employed, death results; but pure urea, when injected, does not give rise to ill effects, no other change being observable but diuresis.

Feltz and Ritter also observed that vomiting and spasm, followed by death, takes place, if the injection of urea be made when food is withheld, and that the same effects are obtainable if it be made in animals whose ureters have been previously ligatured.

Zalesky has produced coma by tying the ureters of birds and serpents. In these creatures, the renal excrement is composed almost entirely of uric acid; urea is present only to a very small extent. It seems unlikely, therefore, that the results which they obtained were produced by its retention.

Peabody found that it is necessary to inject an amount of urea, varying from $\frac{1}{30}$ to $\frac{1}{100}$ of the weight of a dog, to produce convulsions in that animal; and that before convulsions would result in man, urea, to the amount of at least one-and-a-half pounds, must have accumulated. An examination of a patient who had died with

uræmic symptoms, showed only ·009 lbs. of urea to be present.

Bouchard calculated that $\frac{1}{7}$-th of the toxicity of the urine is attributable to urea; he adds, that death follows intravenous injections of urea, as it does after the introduction of several other bodies, which in like manner modify the conditions of osmosis by increasing the density of the blood, and other fluids of the body, to such an extent, that nutrition is hindered. He further noted the lethal dose of a solution of urea to be 122 c.c. per kilogramme of animal; that is, solutions of urea, when injected into the veins of a dog, produce death in exactly the same dose, as does an injection of distilled water.

Snyers found that an injection of urea, equivalent to that which a dog excretes in three days, can be given to it without producing any ill effects.

Taking Bouchard's figures, and assuming that urea is the only toxic substance in normal urine, then death would only result after complete retention extending over nineteen days.

Turning to the evidence afforded by clinical experience, we find cases described by Owen Rees, and Bright, in which the blood contained large quantities of urea, and in which uræmic symptoms did not occur. Biermer's celebrated case, already referred to, showed no uræmic symptoms during the period of suppression, but upon the re-establishment of the secretion, then the signs of uræmia developed. The fact that uræmia sometimes occurs, when the excretion of urea is in excess of the normal quantity, tells strongly against any theory which attributes uræmia to the retention of urea. In some cases of hepatic dis-

order, in which the formation of urea is checked, a development of uræmic symptoms is not uncommon.

In fact, an unprejudiced consideration of Wilson's theory can have only one result :—The absolute rejection of any claim of urea, *per se*, to produce the classical signs of uræmia. Indeed, it seems certain that the part it plays in the complex poisoning, which produces this state, must be very insignificant.

FRERICH'S THEORY. — Frerich, regarding Wilson's theory of the etiology of uræmia as improbable, suggested an ingenious modification. Urea could no longer be looked upon as a toxic substance worth considering, still, Could it not undergo its most frequent decomposition within the body and so become harmful? It is well known that in stale urine urea becomes converted into ammonium carbonate, frequently too, that this transformation takes place within the bladder in patients suffering from cystic disease. To suppose the same decomposition occurring in urea, before it reached the bladder, within the system in fact, did not seem outrageous; and moreover, certain clinical observations, and experiments, made upon the lower animals, seemed to countenance this surmise.

The conversion of urea into ammonium carbonate is due to the action of a ferment which, Demjankow showed, brings about uræmic convulsions if injected into the blood of nephrectomised animals.

Stale urine causes death in less time than perfectly fresh, when injected into the veins of a rabbit.

Spiegelberg, and Geschedlen, found an increase of ammonium carbonate in the blood of a patient suffering from puerperal eclampsia.

Ammonium carbonate, many have asserted, is found to be increased in the blood of uræmic patients, and in normal urine, there is a trace which is also increased in this condition.

A tumbler moistened with hydrochloric acid, and held before the lips of a person suffering from uræmia, becomes filled with the fumes of ammonium chloride; and in the vomit there is often detected a strong ammoniacal odour.

Finally, Feltz and Ritter have produced symptoms resembling uræmia, by the intravenous injection of ammonium carbonate into dogs.

There are several fatal objections to Frerich's theory, the first being, the total absence of evidence that urea ever does become converted into ammonium carbonate, in the blood of a living animal. It is denied that there is any appreciable increase in the blood of patients dying with uræmia. There is a *post mortem* change, which takes place in the tissues, resulting in a production of ammonium carbonate, and this production occurs independently of the cause of death.

Stale urine, when injected into the veins of a dog, owes its increased toxicity to another cause than the conversion of its urea into ammonium carbonate.

The ammonia found in the expired air of uræmic patients, is not peculiar to this condition; its production depends on a dry state of the mouth, and the decomposition of fragments of food contained therein.

Snyers showed, that after ligature of the ureters of dogs, only insignificant traces of ammonia were detectable in the blood.

Voit says that sulphate of soda, or magnesia, are quite

as efficient in producing convulsions, as ammonium carbonate.

Rommelaere, whilst agreeing that there is an increased quantity of ammonia in the blood of nephrectomised animals, shows that the total amount is quite insufficient to produce any symptoms.

Feltz and Ritter have finally disposed of Frerich's theory: they admit that ammonium carbonate, if present in sufficient quantity, would produce uræmic symptoms; but they show that the conversion of urea does not take place within the system. An injection of urea into the vein of a dog, was excreted as such in its entirety during the following twenty-four hours, and there was never more than a trace of ammonia in the urine.

STANNIUS AND TREITZ THEORY. — Stannius and Treitz, to meet the objection that urea never becomes converted into ammonium carbonate whilst within the system, suggested an elaboration of Frerich's theory. They believed, that urea is excreted first into the intestinal tract, in the mucous membrane of which it becomes decomposed, and is from thence re-absorbed as ammonium carbonate.

This hypothesis at one time received considerable favour. Jaksch, and Bernard, both lent to it their support. Ammonium carbonate is constantly found in the fæces and vomit of uræmia; and it is also a highly diffusible salt. It had already been shown that injections of ammonium carbonate produce uræmic convulsions, so it seemed probable that its absorption and diffusion was their cause. Against this theory are arrayed all the facts which tell against that of Frerich, and there are others which can be applied especially to this.

Bouchard resists vigorously the idea that urea is excreted in large quantities into the intestines. He shows, that the ratio of excretion of urea, by the kidney, as compared to water, is 52·1, whilst its excretion through other organs is at the same rate as water. As blood contains only a small proportion of urea, it cannot carry to the intestines a sufficient quantity for its excretion, and re-absorption as ammonium carbonate, to produce any symptoms resembling uræmia. Moreover, to suppose that it is necessary to account for the ammonium salts in the intestine, by pre-supposing the excretion of urea, and its subsequent conversion, is quite gratuitous, as there is always a large amount of ammonium salts in the fæces. Bouchard further points out, that the hypothermia following an intravenous injection of normal urine, is lost by first filtering through a bed of charcoal. Ammonium carbonate is present in the filtrate, and therefore this property must belong to some substance other than it, which has been retained by the charcoal.

Both Frerich's theory, and the modification it has undergone at the hands of Stannius, and Treitz, are now by general consent abandoned ; and as there are so many conclusive arguments against both, and so little to be said in favour of either, any recrudescence would seem improbable.

SCHOTTIN'S THEORY.—As long ago as 1853, Scherer, and Schottin, suspected that the substance, which is responsible for the production of uræmia, might belong to that group of bodies known as extractives.

Oppler soon came forward with some evidence which also seemed to point in the same direction. He showed that animals, which have been nephrectomised, exhibit

an increase of creatin in their blood. Hoppe Seyler observed a like increase, which, he said, amounted to five times the normal quantity, in the blood of a patient who was suffering from cholera with uræmic convulsions.

In the same class of cases, Chalvet noted a decrease in the quantity of extractives in the urine, contemporary with a diminished toxicity of the secretion, as tested by intravenous injections into dogs.

The fact, which physiologists have pointed out, that the antecedent of urea is possibly creatin, seems to lend probability to the assumption, that in uræmia the formation of urea is checked at one of its early stages; with the result, that creatin, its forerunner, accumulates in the blood, and tissues.

Evidence that too much importance was being attached to creatin, was then brought forward by Meissener, who injected large doses of this substance into the blood of dogs, and produced symptoms which were unlike the most usual form of uræmia caused by an injection of the total urine, for convulsions predominated. The chief effect of creatin seems to be that of a muscle poison; the latent period of contraction becomes much prolonged, and the contraction itself is feeble, and is quickly exhausted. Vomiting very commonly results from only a small intravenous injection of this substance.

Feltz and Ritter, however, administered the *coup-de-grace* to Schottin's theory. They injected into the veins of a dog, in one dose, an amount of creatin equivalent to seventeen days' secretion, and death did not result. Death occurring within three days of complete anuria, therefore cannot be attributed to the poisonous properties of this agent, which are, in fact, only equal to those of urea.

Creatinin has also been suspected. This substance is a dehydration of creatin, and occurs in very variable quantities in the urine; being entirely absent in starvation, and much increased when a flesh diet is taken. On an average ·9 grammes are found in the urine per diem.

Feltz and Ritter, disposed of the imputation that creatinin is the toxic agent, by injecting an amount of this substance, equivalent to six days' excretion, into the veins of a dog, with no result. An injection of thirteen days' excretion, however, produced death. Even in this latter case doubt is thrown upon the obvious inference; for it has been shown, that the simple salts of creatinin are hardly injurious, and that the pure substance owes its toxic power to its pronounced alkalinity.

Ranker and Schiffer substantiated the experiments of Feltz and Ritter, by introducing large quantities of creatinin, with no fatal result.

When it is recollected that creatinin is probably formed *in* the kidney, it will be understood that it is not likely to be absorbed from thence in sufficient quantity to produce any very great toxic effect.

Neither leucin, nor tyrosin, are toxic at all; xanthin, hypoxanthin, and guanin, do not possess poisonous properties of any moment. In doses of ·5 grammes taurin is not toxic.

Uric acid, which is normally present in the urine to the amount of ·0084 per kilogramme, cannot be suspected; for, when the system is surcharged with this substance, the symptoms of gout appear, and not those of uræmia.

Haig asserts, that the retention of uric acid causes an increase of the blood pressure, headache, insomnia, and malaise, which are frequently associated with uræmia.

But injections made by Bouchard, of uric acid, far in excess of the amount equivalent to the excretion which takes place in the quiescent period of anuria, produced no toxic symptoms.

Hippuric acid is present in health at the rate of ·006 grammes per kilogramme. Bouchard injected 4·599 grammes, which is an amount equivalent to the quantity formed in one hundred days, and this, producing no ill effects, showed the improbability of it being the origin of uræmia.

Meissener injected large quantities of succinic acid, and came to the conclusion that the pathogenic cause of uræmia must be looked for elsewhere.

Landois found that a direct application of creatinin creatin, or the acid phosphate of potassium to the cerebral convolutions of a dog, gives rise to convulsions. Urea applied in the same way seemed inactive, whilst ammonium carbonate, sodium carbonate or chloride, potassium chloride, and leucin produced only slight effects.

THUDICUM'S THEORY.—In many cases of Bright's disease, and in particular, that known as granular contracted kidney, the urine is very light coloured; in some cases it seems almost colourless. Thudicum thought this retention of colouring matter was connected with the onset of uræmic symptoms. He believed that in urine there is only one colouring matter; this he called urochrome, and to it he attributed uræmia. It is now known that even in healthy states several colouring bodies are present, and in those of disease their number is often greatly increased. The additional chromes possess in many cases very toxic properties. We shall see that

those present in normal urine are comparatively harmless.

Maly and others have shown that Thudicum's urochrome is identical with urobilin, and have separated it by precipitation with basic lead acetate. MacMunn believes this substance to be derived from hæmatin, and bile pigment, by oxidation. Hydrobilin, and another allied substance known as "pathological urobilin," do not appear to be the same as normal urobilin. Vaulair and Masius believed that pathological urobilin is stercobilin, but this does not seem to be the case. (*Journal of Physiology*, vol. vi—1 & 2, and vol. x—1 & 2.)

Indican is present in small quantities in normal urine, and is increased when there is constipation, but does not appear to be very toxic. However all this may be, it is certain that the colouring matters of the urine are decidedly toxic. Febrile urines, which are usually highly coloured, are much more poisonous than those of health, and probably owe some of their increased toxicity to the high colouration. In these, the pigments are ten to twenty times more abundant than in normal urines.

It seems probable that in urine there exists a group of little known bodies of the class of chromogens. These are themselves colourless, but are easily converted into coloured substances, and it is likely that a great part of the toxicity of urine resides in them and in the conversions they undergo. But taking into consideration the toxicity of normal urine only, Bouchard found that an intravenous injection of 45 c.c. kills, with uræmic symptoms, 1 kilogramme of animal. He noticed, that filtering through a bed of charcoal reduces this toxicity by nearly one-half. Decolorised bile loses two-thirds of

its poisonous properties by being so treated. He also found that an intravenous injection of urobilin to the amount of 15 centigrammes does not produce death.

Exercise in the open air diminishes the poisonous action of the urine very greatly, and yet the colouration is thereby, if anything, increased, owing to concentration of the urine. Urine secreted during an uræmic attack loses its toxicity, but there is no corresponding loss in the colouration. The urine excreted during intense mental exertion is commonly copious and pale coloured, yet it possesses a high toxicity. On the other hand, the urine formed during night is highly coloured, and yet has only one-half the poisonous properties of that excreted during the day. Until further progress has been made in the chemistry of the urinary colouring matters, it is evident that much advance cannot be anticipated in the investigation of their poisonous qualities. At present, it is impossible to describe the toxicity of these substances except in terms which apply equally to them, and the chromogens, and possibly other bodies contained in the urine.

GAUTIER'S THEORY.—Gautier believes that certain alkaloidal substances, the products or remains of tissue change, and of minute life, are responsible for uræmia. The chemistry of these ptomaines has made much progress of late, owing to the efforts of Brieger, Selmi, Bouchard and others, but notwithstanding this, very little can yet be said of their chemical constitutions, their identification, and separation, being a matter of great difficulty.

These alkaloidal bases closely resemble, and are, in one or two instances, identical with vegetable alkaloids.

Brieger has isolated a number of them from decomposing animal matter, cheese, gelatine and yeast.

Bouchard succeeded in separating several of these bodies from normal urine. He finds, that in decolorised urine there is an organic substance, which is freely soluble in alcohol, and unlike urea, with which it might be confounded, produces narcosis when injected into the veins of a dog.

Another substance, having the property of salivating, is also present; it is freely soluble in alcohol, and is found in decolorised urine, but does not produce death when injected intravenously. This substance has been detected in the liver, and blood of healthy individuals, but is not present in large quantities. It is interesting to note, that Robin has observed salivation as the only symptom of an uræmic attack.

A substance, having the power of producing myosis, is also present in the urine. An injection of 10 c.c. produces this symptom. The body, whatever it is, must be therefore fairly powerful. It resembles the colouring matters in being retained by charcoal filtration, and in being insoluble in alcohol.

Another substance, which similarly resembles the coloring matters, is also found, its physiological activity is less than, and antagonistic to, the narcotic substance already mentioned.

Hypothermia is a symptom common to many cases of uræmia, and seems to be produced by some heat-reducing substance which, Bouchard has said, is found in the urine. The temperature is lowered by diminishing the heat production and not by favouring its loss. So far as is known, this substance resembles the coloring matters,

and perhaps is one of them, as it is organic, retained by filtration through charcoal, and insoluble in alcohol. It is certainly quite distinct from any of the foregoing, which is shown by the degree of hypothermia not being commensurate to the intensity of the convulsions, and other symptoms, which occur in uræmia, and which are caused by the action of the other alkaloidal substances.

Carter has pointed out that some of the symptoms may be due to ptomaines allied to choline ($C_5H_{15}NO_2$) and neurine ($C_{15}H_{13}NO$). Choline is a compound ammonium base, having three atoms of hydrogen replaced by methyl, and one by oxyethyl, is one of the constituents of lecithin, and is found after the first few days of putrefaction. It then decomposes into tri- and dimethylamine and triethylamine ; its poisonous qualities are similar to, but less than, those of neurine and muscarin (Payne). Neurine ($C_{15}H_{13}NO$), which is obtained from meat after five or six days' putrefaction, is probably derived from cholin, and lecithin ; it is poisonous to mammals in very small doses producing salivation, dyspnœa, acceleration, succeeded by slowing of the heart, violent diarrhœa, and death accompanied by convulsions and collapse.

Peptotoxine is certainly present in the intestine, as it is formed during the digestion of fibrinous material by the gastric juice. Given to dogs it quickly produces paralysis and narcosis.

Bouchard, to whom much of the foregoing is due, in concluding this subject, lays great stress on the fact, that, the organic substances at present known in the urine, are not in sufficient quantity to produce uræmic symptoms. In fact, the total alkaloids which are found in the urine

of man within twenty-four hours would not be enough to kill a rabbit if they were injected into its veins.

FELTZ AND RITTER'S THEORY.—Feltz and Ritter have rejected all the foregoing theories, and have suggested a hypothesis of their own, which looks to potassium salts as being the exclusive cause of uræmia; these they assert are retained, owing to the defective action of the kidneys, and are responsible for any form which uræmic symptoms may assume. They recognise that the amount of potassium salt in the urine is insufficient to cause death within three days, which, when it occurs within that period after the establishment of complete anuria, they say is attributable to some other cause than the toxic action of any single or combined constituent of the urine.

Glancing at the physiology of mineral salt excretion, we find Parkes says, that a man in health, weighing 66 kilogrammes, excretes 1,500 grammes of water and 72 grammes of solid per diem. Of this latter 52·3 grammes are organic, and about 20 grammes inorganic substances, these last consist of about 3 grammes of the salts of magnesia, and 5 grammes of the salts of potassium, whilst the remaining 12 are those of soda.

Feltz and Ritter, by means of an injection of the inorganic salts, have obtained the same symptoms which result from the injection of fresh urine. They proved the potash to be the most toxic of any mineral salt contained in the urine. Precautions were taken that no increase in the blood pressure should be the result of the experiment, so that no fallacious reasoning which might arise on that ground is possible.

Astaschewsky produced "violent uræmia," by injecting

a solution of potassium chloride into the veins of a dog whose ureters he had previously ligatured.

Clinical corroborative evidence for this theory was supplied by D'Espine, who noticed a rise in the quantity of potassium salts in the serum during uræmia, which occurred in a case of scarlatinal nephritis.

Rosenthal, looking upon uræmia as the result of complex poisoning, believes potassium chloride to be responsible for the vomiting, which is frequently present, whilst Rovighi says that the respiratory troubles are to be accounted for by the retention of the salts of potassium.

Aubert found that 85 per cent. of the toxicity of normal urine depends upon its mineral salts.

On the other hand, Snyers and Bouchard, whilst assenting to the toxic properties of potassium salts, believe that their rôle in the production of uræmia is of much less importance than has been asserted. By temporary compression of the renal vessels Lépine produced a diminution in the quantity of solids which was excreted, and notably in the phosphates, but the chlorides were increased. Snyers found ·206 per cent. of potash in the blood of a patient suffering from puerperal eclampsia. This result is quite the reverse of that which would be expected, if the symptoms depended upon its accumulation.

Bouchard conducted a systematic study of the toxic properties of potassium salts. The phosphate, sulphate, and phenylsulphate of potassium, present in the urine, he found to possess less toxic effect than the chloride which was decidedly the most poisonous of all; an intravenous injection of 18 centigrammes per kilogramme

of animal tissue produced death. The sulphate ranks next in toxicity ; but the phosphate is only very slightly poisonous. Of this latter, it is necessary to inject 26 centigrammes per kilogramme. He showed that 45 c.c. of urine is fatal to one kilogramme of animal tissue, and this quantity contains 14 centigrammes of potassium salts. If the potassium salts, equivalent to those present in 50 c.c. of urine, be injected, no ill effects are observable ; but an injection of an equivalent of 100 c.c. per kilogramme causes death. Moreover, the effects obtained by an injection of potassium salts, are not identical with those following an injection of urine, or with the symptoms of uræmia.

Mitscherlich's table of toxicities, as given by Lauder Brunton, is a classification of the various groups of elements, according to the poisonous properties of each. In this list potassium salts are found grouped with those of ammonium, as muscle poisons, and convulsants. It is precisely in this form that the symptoms which follow an intravenous injection of potassium salts take place. They are, in the first place, true muscle poisons and produce the effects of muscle poisoning. An injection of urine which is excreted during the night causes convulsions, whilst that excreted during the day produces coma, and as the effect of an intravenous injection of potash salts is always constant, both these different results cannot be referred to them. Further, filtration of the urine through a bed of charcoal separates the colouring matter, and some of the organic substances, but allows the potash salts to pass through almost in their entirety. An injection being made of the filtered solution it is found that the filtrate has lost rather less

than one-half of its former toxicity ; and, therefore, some substance, which has been separated by filtration, is responsible for nearly half the poisonous action of the urine ; and this substance cannot be the potash salts nor indeed any mineral saline.

Bouchard believes that some pathological urines, which are markedly convulsive, owe this property in a great measure to the potassium salts which they contain. In febrile urines these salts are doubled or trebled. They may be derived from alimentary sources, or be the result of disassimilation of the tissues, but no matter whence they originate, no amount of potassium salt circulating in the blood produces the salivation, and athermia seen in many cases of uraemia.

Of the other mineral salts, those of soda have been shown not to be very toxic, chloride of sodium being the most poisonous, yet an injection equal to one day's excretion kills only about two kilogrammes of animal tissue, whilst an injection of the whole of the urine causes the death of at least thirty kilogrammes.

The calcium and magnesium salts, which are found in the urine, are present only in small quantities, and possess but a low degree of toxicity. An injection of an amount far in excess of three days' excretion produces no effects.

Concerning the group of bodies called "conjugated sulphates," but little is known. They are present in very variable quantities in *normal* urine, and so far as examined, those found in health are not possessed of any decided poisonous action.

Rademaker, in 1891, noticed in the urine of a patient who was suffering from renal disease, the substance

urethane, this he suggested might be the cause of uræmic coma.

By urethane, he probably wished to designate ethyl carbamate, the term urethane being a generic one signifying the ethereal salts of carbamic acid; it should, therefore, not be used to identify any individual member of that class. Schmiedeberg first observed that ethyl carbamate causes narcosis when administered in large doses to warm-blooded animals, and he introduced the substance for this purpose as a drug. It has not been detected in any considerable quantity in the blood of uræmic patients, and it is not always present in albuminous urine. In urine, which has become alkaline from any cause, ethyl carbamate is frequently found; in freshly excreted urine, albuminous or not, it is present only in a small quantity but more often is entirely absent. Experimental doses of one drachm administered by the mouth, produce only a slight hypnotic effect. The drug is found unchanged in the blood, and urine.

Bouchard, who has probably done more to clear away the mists of uncertainty which overhang the pathogenesis of uræmia, than any other investigator, believes that there are four different sites of origin of the poisons which render the urine toxic. These are, Firstly, food substances and drugs; Secondly, intestinal decomposition, the results of which are in some measure absorbed into the blood and excreted in the urine; Thirdly, the secretions—saliva, bile, etc., bile being the most poisonous of these; Fourthly, the substances which result from metabolism. That each, and all these four sources of poisons are efficient has been demonstrated by his untiring efforts. It is important to know the agents

by which the manifestations of uræmia are produced; but it is equally important that the origin of these various toxic substances should be pointed out, for by such knowledge an inkling is obtained indicating the direction that true therapeutics and prophylaxis must travel.

BROWN-SÉQUARD'S THEORY.—The theory brought forward by Brown Séquard deserves some consideration.

He contended that the kidney functions are not entirely those of excretion, that along with this process there goes a no less important one, viz., the elaboration of an internal secretion, which is highly necessary to health.

The suppression of this function, he asserts, is responsible for uræmia, whilst the accumulation of toxic substances within the organism has little or no influence in the production of the uræmic symptoms.

In support of his view Brown-Séquard asserts, that the symptoms of uræmia occurring in dogs which have been nephrectomised, are alleviated or temporarily removed by the injection of an extract made from kidney substance.

This theory accounts for some anomalies which are difficult to explain by a chemical hypothesis; for example, there is frequently a notable absence of uræmic symptoms during a prolonged period of complete anuria. In such cases, Brown-Séquard says, there is sufficient healthy kidney substance left to form an amount of secretion capable of neutralising the poisonous properties of the accumulating urinary substances. His theory would also account for the symptoms which follow ligature of the ureters; these, Broadbent says, often run a different

course, end differently, and are entirely unlike those of uræmia.

Whatever may be the truth of Brown-Séquard's assumption that the kidney is more than an excretory organ, it has yet to be proved that the internal secretion claimed for the kidney, possesses the properties assigned to it. It may be noted, in passing, that "remissions and temporary alleviations" of uræmic symptoms frequently take place in uræmia, without the administration of kidney extract being resorted to. Moreover, an injection of normal urine into the veins of an animal produces precisely the same effects, whether there be a simultaneous injection of renal extract or no. The renal extract may not possess the same properties as does this hypothetical secretion of the kidney; still, the experiment disposes of one of Brown-Séquard's arguments, and gives rise to a suspicion, that his other observations may not be entirely trustworthy.

OPPLER'S AND OSTHOFF'S THEORIES.—Oppler believes that uræmia results from an interference produced by defective kidney function in the regular chemical changes, which take place in the tissue cells and their environment. In what direction this function is defective is not stated, neither is the means by which the interference with the metabolic life of the organism is effected. This interference admits obviously of being brought about by central nervous agency, or by local action; but, however it may be caused, he asserts that it becomes evident in the defective nutrition, anæmia, and functional disturbances of all the organs, including the brain which occur in prolonged kidney disease.

Osthoff believes that a reflex excitation of the vaso-motor centre, is caused by stimulation of the terminations of nerves situated in the kidney, or by a like stimulation of the splanchnics ; and that this interference with vaso-motor control leads to defects in the nutrition of the cellular life of the organism, so giving rise to the manifestations of uræmia.

If Osthoff's theory be correct, an explanation of the production of certain cases of puerperal eclampsia, in which there is no kidney disease, would be afforded. In these cases, the exciting cause lies in the size and weight of the uterus, the predisposing one in that peculiarly sensitive and irritable state of the nervous system, so well known to be a feature of the later months of pregnancy.

THE STATE OF THE BLOOD IN CHRONIC BRIGHT'S DISEASE.

Very numerous have been the attempts to identify in the blood some substance or substances, which might be fixed upon as an efficient cause for the production of the uræmic condition. An advance of our knowledge of the corpuscles themselves is now being made. Whilst from the oldest times, the quantity, and quality of the fluid portion of the blood has formed the object of many a carefully carried out investigation, the corpuscular element has either baffled research, or has been lightly passed over as being of minor importance.

In a great measure owing to the exertions of modern investigators, and especially to those of Kanthack and Hardy, some acquaintance is now being obtained with this group of blood components ; but an application of

such recently acquired knowledge has yet to be made to most diseases associated with an abnormal blood state.

The anæmia of chronic renal disease is often profound. Leichtenstein noticed that hæmoglobin was reduced, in one case, from 1,330 to only 802, whilst there is also a reduction of the red blood corpuscles ; Dickinson has seen the number reduced from 5,000,000 to 3,921,875, and a much less number than this may be observed (Rosenstein 3,000,000).

The amount and quality of the fluid constituents of the blood has already been referred to, so that the changes which take place in the leucocytes may be considered forthwith.

From my observations it seems that one of the most constant changes, affecting the white blood corpuscles in cases of advanced chronic renal disease, is a distinct decrease in the relative number of the hyaline cells of Kanthack and Hardy (the macrophagocytes of Metchnikoff), when compared to the other varieties of white blood corpuscles.

These cells in a normal state are never numerous, Kanthack says they form about 2 per cent. of the whole, but in advanced renal disease, they seem to be almost entirely absent. In health, they exhibit phagocytosis and vigorous amœboid movements.

Another change observable, is the diminution in the numbers of the finely granular oxyphile cells, which normally constitute from 20 per cent. to 70 per cent. of all the leucocytes. These cells also shew amœboid movements, and phagocytosis.

On the other hand, there is an increase in the number of lymphocytes, which seems to make up in some

measure for the deficiency in numbers of the other kinds. So far, I have not been able to observe any constant relative changes in the numbers of the other varieties of leucocytes ; but Dr. Kanthack tells me that Von Lonibeck has noted an increase in the coarsely granular cells.

Analogy would furnish strong support to the inference that these changes are due to the influence of some poisonous excrementitious substance which circulates in the blood of renal patients. It is especially noticeable, that the eminently phagocytitic leucocytes, and those shewing amœboid movements most strongly, suffer the greatest diminution in numbers, and to an extent not proportional to that of the other varieties of leucocytes.

Accepting Ruffer's dictum, that, the various kinds of leucocytes are merely varieties in the development of one form, it will be seen that this condition is just that which might have been expected to appear in a toxæmic state.

Ruffer shewed, that a drop of a culture of bacillus pyocyaneus, injected into the anterior chamber of the eye of a rabbit, produces a migration of leucocytes from the neighbouring blood vessels ; but that if the toxines, derived from such a culture, be first injected into the blood no diapedesis follows the introduction of the culture into the eye as before.

It is demonstrated, in this case, at least, that the loss of phagocytitic, and amœboid tendencies, is caused by the circulation in the blood of a poison, which is the product of cellular life, and it seems likely that a similar loss, which occurs in cases of renal incompetence, results from the circulation of renal poisons which are also in part derived from metabolic activity of cellular life.

That there is a diminution in the power of resistance to inflammatory attacks in Bright's disease, is well known, and that, cases of erysipelas and peritonitis, etc., are especially dangerous when so complicated. Now, this peculiarity could quite well be accounted for, if further research shews that the observations just made are correct : viz., that the members of the class of leucocytes, whose special function is to cope with the agents of inflammatory attacks, are rendered less useful, probably through the paralysing action of certain products of tissue change which ought to have been excreted by the kidney.

SYMPTOMATOLOGY.

The subjective, and objective indications, which arise in the course of uræmic poisoning, are variable and very numerous. One of the most striking features of this condition is the inconstant character of any particular manifestation of its presence. In the course of a few hours a complete change of the whole, or part of a group of symptoms is a common occurrence, rendering a satisfactory attempt at classification of the attack almost a hopeless proceeding.

Regarding uræmia as a group of nervous accidents occurring in the course of defective renal elimination and neglecting any symptoms not apparently the primary effect of the nervous disturbance, the signs of uræmia may be roughly divided into various groups, according as the prominent symptom shewn is associated with the nervous, gastro-intestinal, cardiac, or respiratory systems. It is not suggested that combinations of these different groups do not frequently exist, the reverse being the truth ; but, as each group represents

probably, the predominance of a corresponding excrementitious substance or substances in the organism, it is well to endeavour to disassociate them as much for the purpose of simplicity, as for the purpose of aiding an identification of the causative agent or agents of each type.

THE NERVOUS GROUP.—The predominance of the nervous element in the symptoms of uræmia characterises this group, which is, perhaps, the commonest exhibited. It comprises headache, giddiness, sleeplessness, mania, twitchings, convulsions, coma, spasms, hemiplegia, aphasia, amnesia, amaurosis, hemianopia, loss of taste and smell, and derangements of sensation.

HEADACHE AND SLEEPLESSNESS.—These symptoms are often associated. The headache of uræmia is very variable, sometimes it is severe, continuous, and liable to exacerbations; at others, it is not intense and there are frequent intervals of remission. Concerning its usual localisation there is some difference of opinion. Gowers thinks the frontal region is the most common site, but it is usually stated to occur most frequently in the occipital region, or behind the eyeballs (Osler). It is noticeable that alcohol in any form increases the pain which, if continuous, is exceedingly distressing, rendering sleep impossible, and occasionally producing mania.

Sleeplessness commonly accompanies or precedes the headache of uræmia; it may be the first symptom complained of, and so lead to the detection of the kidney disease.

These two signs of uræmia are especially associated with acute nephritis, chronic exudative or non-exudative nephritis, and also with puerperal eclampsia.

GIDDINESS.—Giddiness is one of the most frequent symptoms of uræmia, and it is often so severe that sickness results. The vertigo is objective and occurs more or less in paroxysms, or it may be continued for several days. Relief generally is obtainable by lying down and closing the eyes, thus distinguishing it from the vertigo of gastric disturbance. It occurs in any form of advanced kidney disease, but is especially met with as a premonitory symptom of puerperal eclampsia.

MANIA.—Mania occurs occasionally as a result of uræmic poisoning, sometimes independently of any other symptom ; but more frequently, it is preceded by violent headache, mental confusion, etc.

The character of the attack is not constant, sometimes there is violent excitability and screaming, and at others it is of the suspicious variety, and associated with hallucinations, and delusions of persecution.

Berger publishes a case of furious-mania which lasted four months. The patient finally died convulsed. There is occasionally in these cases a concomitant rise of temperature, which is often severe. Wagner records a case of convulsive uræmia, in which each convulsion was succeeded by violent mania, and the temperature rose to 107·4 F.

Sir J. Simpson thought uræmia was the cause of puerperal mania, but later investigation has shewn that albuminuria is rarely present in this condition, its absence Simpson tried to explain by asserting that with the onset of mania albumen disappears from the urine.

Savage relates a case in which albuminuria was present only during the period of maniacal excitement ; but the absence of albumen during the outburst and its

re-appearance when the attack has passed off is not uncommon.

From uræmic mania there is generally a recovery in such cases as are dependent on pregnancy, but should renal incompetence be established the final catastrophy is but postponed, sooner or later death usually takes place and is generally preceded by convulsions.

TREMORS AND CRAMPS.—Tremors and cramps are common occurrences in the severe forms of acute and chronic nephritis, and also in puerperal eclampsia.

Delafield believes that they are especially well marked in cases of advanced chronic exudative nephritis. Jaccoud has described a form of cramp :—Tonic spasm of the flexors of the forearm, associated with a like condition of the muscles at the back of the neck, this he says is specially shewn by uræmic patients.

Tremors, cramps, and twitchings, of the various muscles, chiefly flexors, are commonly the forerunners of an outburst of uræmic convulsions. They may be unilateral or may affect particular groups of muscles. When observed in renal disease, they are always a danger signal and an indication of extreme importance.

CONVULSIONS.—Sometimes uræmic convulsions occur without any premonitory symptoms, or are preceded by such vague indications of ill-health that special attention is not directed to them, so that the "uræmic fit" is frequently the first intimation that is received of the serious condition of the patient's health. If, however, enquiry be made, some of these minor indications will usually be found to have presented themselves.

The early recognition of prodromata is of the greatest importance, as active interference in the right direction

is urgently called for, and not unfrequently results in such a manner that an impending attack of uræmic convulsions is postponed, or averted.

Violent headache, persisting for some time, and especially hemicrania occurring in the course of renal disease, are amongst the most frequent signs of an impending attack of convulsions.

Vertigo, epigastric pain, and sickness, are always suspicious symptoms in renal patients. Subjective spots before the eyes, tinnitus, cramps, tremor, twitching, amaurosis, perversions of temper, and general irritability are also frequently premonitory symptoms.

In a case which came under my notice the only premonitory symptom was volubility. The change in temperament shewed itself in the following manner. One evening the patient commenced to read aloud several chapters of an uninteresting work to his assembled family; and in spite of the protests, and inattention of his audience, he continued doing so until a late hour. This he had never been known to do before. Uræmic convulsions came on soon after going to bed, and death, preceded by coma, took place two days later.

Uræmic convulsions are generally sudden in their onset and resemble epilepsy in their course.

They are ushered in by a short period of tonic spasm, which is soon followed by clonic convulsions, in which there is frequently grinding of the teeth and biting of the tongue, a quantity of frothy saliva accumulates around the mouth, and evacuation of the bowels, and bladder, not uncommonly occur.

During the stage of tonic spasm the face assumes a deathly pallor, a cold sweat breaks forth, and there is

intense rigidity of all the muscles of the body. At length, when the patient appears at the point of death, clonic convulsions supervene. These may be general, involving the whole body and of great violence. Cases of spontaneous fracture have occurred during this stage.

Rosenstein, and Strumpell, have recorded hemilateral convulsions only; and Lichtenstein says he has seen trismus and tetanus in this condition; whilst Jaccoud has noted a tonic spasm followed by contractions of long duration, and affecting chiefly the dorsal muscles; this variety is known as Jaccoud's tetanic uræmia.

Brissaud notes, that upon recovery from uræmic convulsions catalepsy sometimes occurs.

Respiration during the period of tonic spasm is arrested, by reason of the general rigidity of the respiratory muscles; and, upon this passing off, breathing is at times irregular and hurried.

Lecorché noted noisy, and sibilant breathing, as a peculiarity of this state.

The convulsive stage fortunately does not last long, usually after a few minutes, the patient passes into a condition of stupor, more or less profound, from which it is generally possible to momentarily arouse him.

The convulsions may consist of only one paroxysm, or may be frequently repeated; in some severe cases there hardly seems to be any interval between each attack, and death occurs at length from heart or respiratory failure.

Uræmic convulsions are commonly met with :—

(1,) In all forms of acute nephritis; especially when this occurs in children, in whom it seems that convulsions are easily induced, and in whom their presence is not so portentous as when occurring in older persons.

(2,) In chronic exudative nephritis, especially in advanced cases. The convulsions supervene on a temporary increase of renal congestion, causing diminished functional activity.

(3,) In chronic non-exudative nephritis. In this state uræmic convulsions are common, either early or late in the disease ; they are particularly ominous, and it is noteworthy, that the liability to suffer from convulsive attacks, is not proportional to the extent of kidney failure.

(4,) In pregnancy with co-existent nephritis, convulsions are always an ever present danger, both before, during, and after delivery has taken place. In a few instances in which they have occurred at this time, nephritis has been shewn not to be present. Some of these cases are not of uræmic origin, and, perhaps, are ordinary epilepsy ; others are the result of the irritation caused by the weight and size of the pregnant uterus, acting along with certain concomitant states, to which reference has already been made.

The diagnosis of uræmic convulsions is not always easy. An examination of the urine will usually shew when kidney mischief is present. The fundus oculi, perhaps, may exhibit signs of albuminuric retinitis. The presence of œdema will also serve as a clue to the nature of the attack. Moreover, although there is great resemblance between epileptic and uræmic convulsions, there are also some differences. In the first place, the initial cry of epilepsy is absent, the pallor of the face is not so marked. The preliminary, and continued turning in of the thumbs, often seen in epilepsy, is not noticeable in this state. The subsequent condition is one of stupor,

rather than the deep coma which is often present after an epileptic attack.

COMA.

This symptom may succeed an uræmic convulsive outburst, or may develop suddenly without any premonitory signs ; in the latter case, the patient passes from a state of apparent health into a comatose condition, preceded only by drowsiness and lethargy. Usually, however, there are some indefinite indications of what is about to occur, these are headache, vertigo, vomiting, delirium, or visual disturbances.

Küssmaul's coma is sometimes met with, it is characterised by an aura of violent gastric pain, rapid pulse, and a peculiar sighing respiration, sooner or later to be succeeded by profound coma.

Uræmic coma is attended by complete unconsciousness. The pupils are generally diverted and widely dilated, occasionally there is considerable myosis. Reaction to light is either altogether lost or greatly impaired. There is injection of the conjunctivæ, and of the face, which, however, may be pallid. Reflex action in profound cases is entirely absent, even swallowing being impossible. The soft palate hangs loosely in the mouth, through the relaxation of the palatine muscles.

Respiration is slow and gasping, and Cheyne-Stokes breathing is more frequently met with in uræmia than in any other condition. Roberts says, that slow and panting respiration is especially associated with obstructive suppression of urine, this, however, does not seem to be strictly correct.

The stertor of uræmia is higher pitched than that met

with in other comatose states, and has been described as hissing, or whistling in character. Owing to imperfect respiratory movements, mucus collects in the trachea, and after a time gives rise to the well known "death rattle."

In deep coma, evacuation of the bowels and bladder may occur: there may, on the other hand, be retention of urine.

The comatose state lasts for an indefinite period, during which it varies in its depth. At times, there seem to be glimpses of returning consciousness, and renewed hope is entertained, only to be often disappointed by relapses into a more profound coma than before.

It is noticeable that coma, occurring in this condition, is often noisier and more restless than a like state associated with other diseases. The patient, when not deeply comatosed, may constantly attempt to get out of bed, or remove the clothes, and delirium of the low muttering type is often present. These two symptoms, restlessness and coma, are of most ominous importance, and usually point to an early close of the scene by death.

Other significant complications are, firstly, a persistent rise in the temperature; a temperature of over 105° is occasionally met with. Secondly, a considerable fall of temperature. Netter observed a temperature of only 86°, and numerous cases have been recorded in which a temperature of 90-95° was present. Thirdly, pneumonia developing in the bases of the lungs is a very fatal complication, congestion of the lungs is one of the most common states found at the autopsy.

Patients suffering from chronic renal affections are generally lethargic. A systematic examination of the reactionary periods of these cases has shewn me an

increase in the "personal equation," which seems to vary roughly according to the density and amount of urine, excreted from day to day. In more than one instance, has this increase in the reactionary period, been one of the first indications of an uræmic attack which was impending. It appears that the reactionary periods of touch, and sound, are more affected in this way than that of the nerves of sight; the former being increased out of proportion to that of the latter.

Death is, perhaps, the commonest conclusion to profound coma of advanced renal disease. In favourable cases a gradual return to consciousness takes place; stupor supervening upon coma, to be itself replaced by heavy sleep, is the usual route taken on the way to recovery. Instead, however, mania sometimes develops, in which death frequently occurs from exhaustion, or the patient upon awakening is found to be in a state of dementia. Neither mania nor dementia, resulting from uræmia, are of long duration, either a relapse occurs into the comatose state or an improvement takes place, commensurate with a like improvement in the kidney function and general health.

The diagnosis of uræmic coma must be made from that of apoplexy, opium poisoning, diabetes, alcoholism, epilepsy, and hysteria.

An examination of the urine, drawn off if necessary with the catheter, should always be made.

The presence of albumen does not necessarily signify uræmic coma, as cerebral hæmorrhage frequently occurs with albuminous urine; but albuminuria in the young, with no cardiac affection, generally points to an uræmic cause.

When hemiplegia occurs with uræmia, the diagnosis from cerebral hæmorrhage is very difficult. Suckling relates an interesting case of a man, aged 40, with the usual signs of Bright's disease, who was seen for the first time semi-comatose and with right hemiplegia. Venesection resulted in a return of consciousness, and a disappearance of the hemiplegia. Five similar attacks followed admission into hospital, and each was preceded by delirium, restlessness, violent convulsions of the face, right arm, and leg, with conjugate deviation to the right side. Chanternesse, and Tenneson, have described similar cases.

Other symptoms present generally enable a diagnosis to be made. In uræmia there is usually a marked lowering of the temperature. In apoplexy a slight lowering is succeeded by a rise.

Convulsions commonly precede uræmic coma, and occur during its continuance; whereas in apoplexy there may be, at first, convulsions, but these are not repeated (Gowers).

Convulsions do not occur in alcoholic coma. Coma associated with rigidity of the limbs, and localised muscular twitchings, if continuous, point to cerebral mischief; but if these symptoms are not localised, then uræmia is probably the cause of the condition.

Coma with considerable glycosuria would point to diabetes being the cause.

The state of the pupils does not afford much assistance; they may be normal or dilated, in uræmia, in alcoholism, and in profound opium poisoning. Inequality usually implies local cerebral trouble. Albuminuric retinitis points to uræmia in default of localised symptoms.

Uræmic coma can be diagnosed from hysteria and malingering, by the absence of the deviation of the eyes in these latter cases.

HEMIPLEGIA, APHASIA, AND AMNESIA.

Hemiplegia and aphasia are occasionally met with. They are sometimes present together, but may occur separately. They are especially associated with the non-exudative form of nephritis.

The onset is often sudden and may or may not be accompanied by coma. When these symptoms are due entirely to uræmic poisoning, they pass off in the course of a few hours or, more probably, days; but the difficulty is to decide how much depends on this condition, for there is generally a high tension pulse, and frequently endarteritis, which are both favourable to an attack of cerebral hæmorrhage. The diagnosis of uræmic hemiplegia is, therefore, often made after the symptoms have cleared up, and, indeed, greatly in consequence of their so doing.

Amnesia is not an uncommon symptom of defective renal function. Brieger has placed on record some interesting cases, in which the loss of memory of words was limited to those expressed verbally, but those that were written were nearly perfectly employed.

The symptom, when due to uræmic poisoning, resembles aphasia, in the speedy manner it disappears, and also in its association with uræmic coma, etc.

DEAFNESS.

Uræmic deafness has been recorded by many authors, Dieulafoy, Rosenstein, Downie, and others. It arises in

like manner to the symptoms just described, depending upon the paralysis of the cerebral centre for hearing, probably brought about by the circulation in the blood of some poisonous material; and it is not due, as was suggested by Downie, to the existence of minute hæmorrhages in the cochlea. Recovery nearly always soon takes place.

BLINDNESS, HEMIANOPIA. — Blindness and other ocular symptoms chiefly occur in advanced cirrhosis of the kidney, and also in acute nephritis and puerperal cases. These defects of vision, when due entirely to uræmia, are not associated with any retinal change which can be made out ophthalmoscopically. The loss of sight may be complete or partial, and may develop quite suddenly, or commence gradually. There is commonly dilatation of the pupils; Wagner contends that they preserve their sensitiveness to light, but Gowers states this is frequently lost, and that they seldom react as readily to light as in a normal state.

This response to light stimulation, depends upon the nature of the attack, and seems to show that the nerve elements, on which the blood state acts, are not always the same. For, when the light reflex remains the poison directly affects the cerebral visual centres; but when there is complete loss of the reflex, it seems that the retina itself must have been rendered insensitive, the uræmic poison acting in this case either upon it alone or upon both the retina and visual centres. Wagner believes the seat of the blindness to be in the corpora quadrigemina in all cases.

Fortunately uræmic visual disorders do not persist for any length of time, and when uncomplicated nearly

always end in recovery taking place within a few hours or days. Förster relates a case of amaurosis which lasted for seventeen days, and finally recovered.

Loss of Taste and Smell.—Loss of taste and smell are sometimes observed and generally more or less associated. They may be noticeable for the first time after uræmic convulsions, or coma, or may develop independently.

A case of chronic granular kidney came under my care, complaining only of these symptoms, which led to an examination of the urine, and so gave the explanation of an apparently causeless condition. The case is related at length in the Appendix.

Hiccough.—One of the most frequent symptoms of advanced renal disease is hiccough. It occurs either as a reflex nervous phenomenon, or as one having a central origin. Only this latter form can be looked on as uræmic. In the former case, the irritation of the terminal branches of the phrenic nerves, situated upon the under surface of the diaphragm, is brought about by some functional disturbance of the stomach, etc. This variety is relieved by vomiting and gastric sedatives. The true uræmic hiccough is, however, a most troublesome symptom, and most difficult to treat. Liveing and Pritchard believe that this form really is a modification of uræmic convulsions. It no doubt depends, as do the spasms and twitching of uræmia, upon some nutritional or vascular disturbance affecting the cerebral centre, in this case the diaphragmatic.

For days and nights, in fact to death itself, this troublesome affection may last ; varying in intensity, but seldom remaining absent for long, in severe cases it soon wears out the strength of the patient.

VARIATIONS IN TEMPERATURE. — In uræmia both pyrexia and athermia are met with. Both are serious complications when pronounced. It is not at present known what substance, or substances, if any, produce pyrexia; but it has been clearly shewn by Bouchard and others, that the urine contains at least one heat-reducing substance.

MacBride (quoted by Saundby), gives the following four conditions as being especially associated with a low temperature :—

(1,) In kidney disease, following affections of the urinary passages, and in complete obstruction.

(2,) In uræmia of old persons.

(3,) In uræmia occurring in old standing kidney diseases complicated by vomiting, diarrhœa, and hæmorrhage.

(4,) In uræmia which supervenes in cancerous cachexia, and marasmus.

The athermia of uræmia is not brought about by an increase in the loss of heat, but by a diminished evolution of heat by the tissues themselves. Hutinel remarks, that athermia in uræmic coma, occurs more frequently in surgical kidney and disease of the urinary tracts, than in coma resulting from other renal troubles. Such temperatures as 86·1 and 89·6 and many from 90° to 95° have been recorded by Bourneville, Roberts, and others.

Pyrexia in uræmia is much rarer than the opposite condition. Lépine shewed that pyrexia was produced by ligaturing the ureters of a dog, and driving the secretion back into the circulation. The conclusion to be drawn is that cases of obstructive anuria should

shew uræmic symptoms with fever. The reverse, however, is the truth, obstructive anuria is generally accompanied by a fall of temperature. Febrile uræmia is always a very serious symptom, but not necessarily followed by a fatal result. In uræmic coma, etc., hypostatic pneumonia and other inflammatory affections are likely to occur; and such complications must be responsible for a certain number of cases of high temperature in this condition. The peculiarity of uræmic variations in temperature lies in the very sudden changes which take place in the body heat, without any cause to which they might be attributed, *e.g.*, a persistently low temperature occasionally gives rise to one several degrees higher than normal, but which after a few hours falls again, and may be as low as before.

HYPERÆSTHESIA OF THE SKIN, AND PERVERSIONS OF SENSATION.—These symptoms sometimes occur, and are generally associated with renal disease in which there is considerable effusion. In granular contracted kidney they are often met with in advanced cases.

The perversions of sensation are especially distressing; formication is the most common of these, and is quite unrelieved by scratching, or indeed by any local application. Numbness, and tingling, are also commonly met with after an attack of uræmic convulsions; they are not very constant symptoms, disappearing usually in the course of a few hours.

Local vascular constriction or dilatation of the vessels supplying the extremities are often noted. The skin of the part affected becomes absolutely colourless and apparently lifeless.

This condition when affecting the hand has been

described especially by Diculafoy, and has received his name, but the "dead white hand" of Diculafoy is seen in other complaints besides renal, and is certainly not pathognomic of defective elimination on the part of the kidneys.

The skin eruptions associated with renal disease are numerous, and it is difficult to separate those which arise from the irritation, caused by an elimination by the skin of certain substances which ought to have been excreted by the urine, from those arising as the result of certain changes in the nutrition of the parts, due to disturbances of the central nervous apparatus.

Renal disease is a powerful predisposing cause of any form of inflammatory skin affection. A dark red, measly-looking eruption is sometimes met with; it is found most profusely upon the back, shoulders, and back of the limbs.

Dermatitis exfoliativa, usually of the moist variety, sometimes occurs, and may be universal, or confined to the arms, legs, and back of the neck. It is decidedly a serious symptom, and especially so when hæmorrhagic.

Liveing has recorded two cases, in which any temporary improvement in the condition of the skin was always associated with a diminution of the quantity of albumen in the urine, and this experience is that of most writers.

Erythema and eczema are both common skin eruptions in renal disease. The latter may be diffuse or occur in localised patches; it is usually met with on the trunk and face, and doubtless depends much upon the irritation caused by the excretion of urinary substances.

GASTRO-INTESTINAL SYMPTOMS.

Catarrh of the stomach, and pharynx, is often present in renal affections, and no doubt in a certain number of such cases depends upon the local irritation, caused by the attempt which the stomach makes to take over some of the functions of the kidney.

Apart from this cause, heart failure, by producing a passive congestion of the organ, renders digestion imperfect, so that the food itself becomes an irritant, and helps to maintain the condition. Voit produced œdema, and congestion of the stomach, by intravenous injections of urea.

Biernocki states that there is a diminution of gastric secretion, and that hydrochloric acid is absent or scanty. The gastric ferment is also diminished, but motor activity is increased.

The symptoms, which are ascribed to this condition, are pain after food, flatulence, nausea, and vomiting, with constipation alternating with attacks of diarrhœa.

Vomiting arises as a result of the foregoing conditions, and also as part of a reflex act from stimulation of the renal endings of the sympathetic nerves. Bartels believes that the œdematous state alone of the gastric mucous membrane is sufficient to induce vomiting, but Cohnheim says that the decomposition of urea into ammonium carbonate within the stomach is the efficient cause.

That vomiting in uræmia is sometimes caused by central nervous disturbance, is also probable, and it may be suspected to arise from this in certain cases of Bright's disease in which there is no great accumulation of excrementitious substances. In children, vomiting in the

course of acute nephritis is very common, and very difficult to check.

Vomiting occurring in the waxy form of kidney disease, is probably due to a like change in the vessels of the mucous membrane of the stomach. (Delafield.) It is in these cases that hæmatemesis most frequently occurs. Hæmorrhage takes place into the stomach, as it does into the other organs of the body, when lardaceous disease is present.

CATARRH OF THE INTESTINES.—The observations made with reference to gastric catarrh, in respect to its etiology, may just as fitly be applied to intestinal catarrh. Like the former it is very common in advanced cirrhotic renal disease, or in the acute inflammatory forms. It is, however, in cases of waxy degeneration that this symptom becomes most prominent; it may be associated with ulceration, and hæmorrhage from the bowel. Whatever may be the cause of the diarrhœa, it is often very profuse, and exhausting; a *post-mortem* examination may shew signs of inflammatory action, which Wagner maintains is always present. Ulceration is not always detectable in cases in which pronounced hæmorrhage has occurred.

HEPATIC AFFECTIONS.—Hypertrophic cirrhosis of the liver is described by Hanot, and the condition has been called by him uræmic liver. Congestion, fatty or waxy disease of the liver, are sometimes present, and atrophy occasionally, but it is very doubtful how much depends upon the toxæmic state.

RESPIRATORY SYMPTOMS.

Dyspnœa is one of the most frequent symptoms

occurring in advanced renal disease ; but it is not always of uræmic origin. The difficulty experienced in breathing may arise from distention of the abdomen by dropsy, impeding the descent of the diaphragm, or from effusion into the pleural cavities. These may be instanced as examples of some forms of dyspnœa occurring in Bright's disease, from purely mechanical causes.

Bronchitis, pneumonia, or circulatory failure are often the causes of other varieties, but reference will now only be made to uræmic asthma, œdema of the lungs, and glottis, as they are especially related to a toxæmic condition of the blood.

How uræmic asthma is brought about in this condition does not seem quite clear, but the prolonged inspiration, and other signs point to spasm of the bronchioles. Delafield, however, thinks the real cause of this symptom is circulatory disturbance. He says that an examination of the coats of the smaller vessels of the lungs will shew chronic endarteritis, and with this there is usually increased blood pressure, and frequently emphysema. Uræmic asthma may perhaps result from a localised spasm of the pulmonary blood-vessels.

This form of dyspnœa is met with most commonly in chronic non-exudative nephritis, but also occurs in other forms of chronic renal disease. It is frequently the first symptom to appear in contracted kidney, and may be present for some time without causing much distress. The early attacks of uræmic asthma take place only after exertion, bodily or mental, and continue for only a short time, but later this symptom becomes extremely distressing ; an attack takes place without the slightest

warning, and may last for many hours. An examination of the chest reveals nothing that can account for its severity.

Howard describes four varieties of uræmic dyspnœa, and they occasionally form a sequence in an attack. They are the paroxysmal, the continuous, the alternating, and Cheyne-Stokes. Of these, Cheyne-Stokes respiration is a phenomenon very commonly met with in kidney trouble, and has already been referred to. It is always a symptom of importance and gravity, but in these cases is not so generally a forerunner of death as when it occurs in other diseases.

It may be present continuously for many days or weeks. West recorded a case in which Cheyne-Stokes breathing lasted for three months, but which ultimately recovered. Cases extending over a week are not very rare, but the most common variety is that which occurs for only a few hours at a time. When this symptom develops in the course of uræmic coma, an unfavourable course may generally be predicted.

Reference has already been made to the noisy, and sibilant character of the respiration of uræmic coma, and also to the character of the breathing in obstructive suppression of urine.

A condition which resembles Küssmaul's coma is met with in renal affections; it is characterised by a peculiar, slow, sighing respiration, and increased cardiac action, which is now shewn to be associated sometimes with an acid state of the blood. The Bradshawe lecture of 1888 contained an interesting case of this kind, in which Dr. Carter noted the blood to be distinctly acid; since then similar cases have been recorded. It has been suggested

that this acid has been absorbed from the intestine, originating there from the decomposition of food; but this substance has not yet been identified.

ŒDEMA OF THE LARYNX.—Reference is here made only to that form of localised laryngeal œdema which depends upon the uræmic state of the blood. Œdema of the larynx is often present as part of a general dropsy, occurring in acute and sub-acute nephritis, and then can be generally attributed to failure of the heart's action.

Localised œdema of the larynx, affecting especially the glottis, and associated more or less with pulmonary œdema, are symptoms which sometimes occur in the latent form of cirrhotic kidney, and appear to be the result of a specific poison affecting the vaso-motor apparatus controlling these parts. This seems highly probable, as similar neurotic dropsies are seen sometimes in anterior poliomyelitis, and in certain affections of the trigeminel nerves. Wooldridge has described a toxin which causes œdema when injected into the subcutaneous tissues.

The symptoms of œdema of the larynx are usually sudden in their onset, and well marked, There is difficulty of breathing, some loss of voice, accompanied by a troublesome cough, which is husky in character. Deglutition is slow, and painful, and in case relief is not obtained, the signs of defective æration of the blood become manifest, and the case probably terminates in suffocation.

A laryngoscopic examination shews exudation affecting first the aryepiglottic folds and the epiglottis; later this extends throughout the remainder of the larynx

with the exception of the vocal chords which usually escape. Not uncommonly inflammatory action supervenes, and then the prognosis becomes exceedingly grave.

ŒDEMA OF THE LUNGS.—In œdema of the lungs both lungs are usually affected, and there is often an accompanying bronchitis, and not uncommonly a subsequent pneumonia.

The onset of the attack is generally sudden, the clinical signs being dyspnœa, retching cough, and copious frothy expectoration, whilst no great pain is complained of. There is dulness, diminished vocal fremitus, lessened respiratory murmur, and fine crepitation. Bronchial breathing, and ægophony are absent. The temperature is never very high unless there is also an inflammatory process taking place.

Œdema of the lungs occurring in the course of renal affections is of the gravest importance; it is commonly the final scene in this condition, but occasionally recovery takes place, and the patient obtains a temporary respite.

CARDIAC SYMPTOMS.

It seems improbable that cardiac hypertrophy occurring in the course of uræmia, can be ascribed to the direct action of an irritant, which has accumulated owing to defective elimination. It is now regarded as a secondary effect caused by increased peripheral resistance to the circulation, throwing extra work upon, and being followed by a compensatory development of heart muscle. Grawitz, and Israel, have at least shewn that cardiac hypertrophy is not the cause of the increased arterial tension; and Mahomed noticed that a rise of blood

pressure precedes albuminuria in scarlatina. It is now generally conceded that the obstruction lies in the capillaries, and that it does not depend upon an arterio-capillary fibrosis, an elucidation which we owe to Ewald. He is inclined to think the obstruction is produced by an alteration in the density of the blood. How this may result has been interestingly demonstrated by Hamilton. Grutzner proved that an intravenous injection of urea produces a rise of arterial tension, which, Grawitz says, results from stimulation of the heart and a quickening of the blood stream. Buhl believes that cardiac hypertrophy succeeds myocarditis when animals are fed upon urea. Senator thinks that contracting kidney is asssociated with concentric hypertrophy, whilst fatty kidney occurs with the excentric variety.

The symptoms of cardiac hypertrophy without any other form of heart disease are not very pronounced; among them, dyspnœa, occurring after moderate exertion, and palpitation, are the commonest. Palpitation is often very severe and distressing; the rhythm of the heart is irregular and intermittent, and the beats occasionally so rapid as to be uncountable.

There is no doubt that this functional disturbance is often due to the toxæmic state and not entirely to the changes in the cardiac muscle, which in many severe cases are not great.

The pulse is irregular and usually rapid, but sometimes is very slow, 50 or less beats per minute may only be registered. It is sometimes full and of low tension, but most frequently is small, hard, and incompressible. A sphygmographic tracing shows very clearly the effect of high tension. The tidal wave is increased in size, and

eventually may be higher than the rise which corresponds to the ventricular close. The apex beat is displaced outwards and downwards. The cardiac impulse is strong and heaving; the area in which it can be felt is increased. The heart sounds are loud, and frequently the first is reduplicated, and there is often an accentuated second, which was first pointed out by Johnson. Murmurs are not uncommon; Bartels believes acute endocarditis to be the direct result of the renal disease.

Heart failure frequently occurs in chronic renal disease of old standing. It is doubtful whether this sudden giving out of the heart can be attributed to central nervous influences, or to the direct action of toxic blood upon the tissues of an already overworked organ. In many instances it results from a break down of compensation, by reason of the increasing weakness of the heart wall from myocarditis. The symptoms are: rapid dilatation of the ventricles, dyspnœa, syncope, pallor, œdema of the dependent parts, and of internal organs.

TREATMENT.

So much can be done by appropriate treatment, towards averting or mitigating an attack of uræmia, that an early recognition of the signs of defective kidney function is of the highest importance.

At the outset, we are met with the fact which Rosenstein emphasizes, that at present we are in possession of no drug which is capable, by its own action, of reducing the amount of albumen which escapes from the kidneys in Bright's disease. Numerous are the remedies which have been advocated to effect this reduction. It has seemed that an exhibition of some has been followed by

favourable results; but further experience has shown that, so far, these results are merely of the *post hoc* nature, from which it is impossible to formulate a generalisation worthy of acceptance.

Although it is at present impossible to successfully combat by the aid of drugs, what may be regarded as one of the chief symptoms of kidney disease, much may be done towards securing a recovery, which is more or less complete, by placing the patient in such a favourable environment, that the smallest possible amount of work is thrown upon the diseased organs. Such observations might seem to apply especially to the treatment of the earlier stages of renal failure, before the effect of toxæmia is manifest, but the principle to be maintained throughout is always the same.

Besides attempts to place the kidney as far as may be in a position of physiological rest, it is advisable to endeavour to counteract the effects of some of the toxic substances, which accumulate in the blood in this condition, and so give rise to local manifestations.

The treatment of uræmia divides itself into general treatment, and the treatment of local symptoms.

GENERAL TREATMENT.—In all cases of Bright's disease, where the quantity of urine excreted is becoming less, or in which the albumen is increasing, or in which any symptoms of uræmia show itself, it is very important that the patient be sent immediately to bed.

It is often surprising how much, rest in bed and simple diet, will cause to disappear many of the unfavourable signs of renal disease, without further treatment. The best diet for patients shewing uræmic symptoms, if they can bear it, is undoubtedly milk, and some of the simpler

farinaceous foods. In severe cases milk alone, diluted if necessary with barley water, or soda water; and if pure milk cannot be borne, then skim milk, or whey, mixed with measured quantities of cream, should be tried. Some authors object strongly to the addition of lime water to milk, and perhaps it had better be omitted unless specially indicated.

Certain foods in uræmia must be absolutely forbidden, especially all forms of beef essences, beef teas, strong soups, etc.; these are veritable poisons in a condition in which the kidneys are already taxed to their utmost. If greater latitude be desired as some of the signs of uræmia pass off, and the quantity, and quality of the urine becomes better, then an addition of known amounts of vegetables and fresh fruits may be made; later, when a more liberal diet is allowed, the effects must be carefully watched by a daily examination of the albumen in the urine. Alcoholic stimulants, if given at all, must be used with great discretion.

When the onset of acute uræmia seems probable, then every effort in our power should be made to check, in any manner possible, the formation of the poisonous material; to hasten its removal from the body, or its destruction *in situ.*

The probable sources of many of these substances we know, thanks to the admirable exertions of M. Bouchard and others. To recapitulate, these are four in number: Those arising from (1,) disassimilations; (2,) the secretions; (3,) alimentation; (4,) intestinal decompositions. The indication is to reduce the formation of poisons at each of these sites to the minimum consistent with life.

(1,) There are several drugs which have been credited

with the power of reducing the metabolic activity of the organism. Bouchard, however, believes that any effort in this direction is unnecessary, as in states bordering upon uræmia, or in which uræmic symptoms have developed, there is already an arrest of disassimilation, as a result of the toxic effects of the excrementitious substances circulating in the blood of the organism; in fact, in this condition cellular life is at a standstill, even oxidation being carried on imperfectly.

With regard to the second source of the uræmic poisons, it has been shown that bile is the most toxic of all the secretions; so that the object becomes in this case, either to reduce the quantity of bile formed, or to diminish its absorption into the system.

Recent research into the action of medicines reputed to be active chologogues, has shown that many of the most prized hepatic stimulants have little, or no influence upon the secretion of bile. On the other hand, those that are supposed to reduce the amount formed by the liver, are equally untrustworthy. The usual secretion takes place after food, and at other times, regardless of any treatment which we may adopt. The least irritating foods, however, seem to cause less reaction of the intestinal tract, and a smaller flow of bile, etc., than do those substances which usually form the elements of an ordinary meal; with this object milk foods are recommended. Bile is nine times as poisonous as urine, volume for volume.

Prof. Bouchard has shown quite clearly that much of this toxicity resides in the colouring matters; of these bilirubin is ten times as poisonous as bile salts, and accounts for two thirds of the total toxicity of the

secretion. He believes that the administration of charcoal causes some decolourisation, and so lessens its toxic influence. With the object of rendering the time occupied in the transit of the bile, and the opportunity of its reabsorption in the intestines, as short as possible, and to prevent its accumulation, a brisk purge should occasionally be given. The effect of this is frequently very marked; many of the minor symptoms of uræmia, not uncommonly, completely disappear. The improvement which results does not depend, however, entirely upon the expulsion of the bile; but also is due in part to the derivative effects of the catharsis; the lowering of the blood pressure; and the removal of certain products to be presently mentioned.

The third source of uræmic poison lies in alimentation. In this connection there must be special attention paid to avoid introducing into the system certain foods, or drugs, which do themselves possess toxic properties. It is for this reason that extracts, or essences of meat, beef tea, soups, meat jellies, or juices, should be especially avoided. All these contain extractives, and other substances, which are identical with the chemical constituents of urine (Masterman).

The brilliant observations made by Feltz and Ritter, leave no doubt but that potassium salts, whether given medicinally, or occurring in the diet in any quantity, are highly dangerous; in fact, the convulsant effect obtained from an intravenous injection of normal urine, Bouchard attributes almost entirely to the action of these salts. Notwithstanding this, bromide and the other salts of potassium, are frequently recommended in uræmic states; but if the knowledge obtained from experimental

physiology is to be thus neglected, if an opinion formulated from experiments so carefully conducted as they were, is to be ignored, then there does not appear to be much hope that medicine will ever be improved, by any advance in the science upon which it should lean.

Finally, an attempt should be made to render the intestinal tract as aseptic as possible. To establish complete asepsis is an impossibility, and if it were possible, it is doubtful whether life could be carried on under such circumstances. Be this as it may, the fact remains that the judicious selection and administration of certain drugs results in such a loss of bacterial growths, that decompositions are reduced to a minimum. The fæces lose their characteristic odour, and the clinical results obtained are certainly far more favourable than those resulting from any other treatment.

To bring about this desirable state, attention must be paid in the first place to the dietary of the patient. It is a happy coincidence, that the diet, which we have seen to be most efficient in reducing the chance of absorption of the secretions, and which contains the least toxic material itself, is precisely that which is most suitable to supplement endeavours at intestinal asepsis: it should, therefore, be adhered to. The selection of drugs which will tend to lessen intestinal putrefaction, demands care. If we knew of any which would not be absorbed, or decomposed, and so rendered inert during its passage through the intestine, then this drug would be exactly what is required. Such an ideal substance, notwithstanding numerous candidates, we do not possess. Rosbach, the sponsor of naphthalin, has to admit, that the brown colouration of the urine which occurs in its

administration, is evidence of its partial absorption; this is clinically shewn by the vomiting, and other symptoms it sometimes produces. At the same time naphthalin is not, itself, a very poisonous body. Seifert has proved that members of this class act in another way besides that of antiseptics. A combination, he says, takes place between them and the toxalbumens, the products of bacterial life, which results in diminishing their poisonous effects. Bouchard found that 40 cc. of urine, from a man suffering from gastric catarrh, killed one kilogramme of animal tissue; but that after an administration of naphthalin, an injection of 100 cc. of urine was harmless. Certainly naphthalin is one of the best drugs we possess for reducing the toxicity of the urine.

The undesirable symptoms—nausea, vomiting, and hæmaturia—which sometimes follow its administration in medicinal doses, probably depend upon the impurity of the drug used. Its taste and smell are, however, decidedly objectionable, but they may be concealed by administering it mixed with sugar, and scented with the oil of bergamot (Lauder Brunton), or it may be given in wafers.

α-Naphthol, C_{10}, H_7, OH, is rather too irritating to administer for any length of time, but is only one-third as toxic as *β*-naphthol. It resembles naphthalin in being an intestinal antiseptic, and may be administered in the form of a pill, as suggested in the *B. M. J.* of '92, page 167. *β*-naphthol, C_{10}, H_7, OH, is rather a dangerous drug to use in conditions where renal functions are at fault. It is, however, a most powerful intestinal antiseptic, far more pleasant to take than naphthalin; and if given in small doses, and the effect watched

the loss of consciousness, convulsions, and hæmaturia, which sometimes result from its incautious use, seldom occur. Benzonaphthol, C_{10}, H_7, C_6, H_3, CO. OH, or, the benzoate of β-naphthol, is a very useful, non-official, intestinal antiseptic It is nearly insoluble in water, but upon entering the intestines it is decomposed into benzoic acid, and β-naphthol ; some of the benzoic acid passes out in the urine, and during its journey through the blood may play a part not altogether useless, as it is said to lessen tissue change, and to reduce the toxicity of the urine ; benzoate of soda is sometimes given to counteract the effect of poisonous products in the blood. The β-naphthol, also set free in the intestines, escapes through the stomach as an inert body, without producing the gastric symptoms which sometimes follow its exhibition as such by the mouth.

Iodoform was strongly advocated by Bouchard, as a means by which decomposition can be held in check. The major portion of a medicinal dose escapes in the fæces unchanged, but part is decomposed, iodine being found in the urine. The drug is not altogether a safe one ; it possesses a powerful effect upon the heart, and occasionally produces death by paralysing its action. It is, therefore, contra-indicated where heart failure is a feature of the renal disease ; generally doses of a half to three grains are well borne, and any objectionable effects, Behring says, may be prevented by a simultaneous administration of sodium bicarbonate, gr. x, repeated every hour.

Salol has been employed with the object of checking intestinal fermentation, and it is one of the most powerful means we possess for this purpose. (*Therap. Gaz.* 1891,

653.) After leaving the stomach, it is split up into phenol, and salicylic acid, both of which are more or less absorbed ; and appear in the urine. For this reason it is not so useful as the more recent introduction, guaiacol carbonate : Hoelscher claims that this substance suffers no decomposition in the stomach, and causes no irritation. Upon entering the intestines it is slowly decomposed (much more slowly than salol), its action continues throughout, and there is but little absorption ; such as there is, is said to be harmless. Iodine, and chlorine waters, have been both employed with the object of bringing about intestinal antisepsis, but have proved inefficient, and are now supplanted by more recent preparations. Charcoal, we have seen, is useful as a decolouriser of the bile, but is also given with the object of precipitating the ptomaines, and so rendering them inert. Frequent purgation is highly necessary to supplement any effort which may be made to prevent intestinal fermentation. It has been shewn that urine loses much of its toxicity if exercise be taken in the open air. The products of tissue metabolism become thereby more completely oxidised, and are thus rendered less poisonous. Jaccoud, with this object in view, recommends frequent inhalations of oxygen ; in some cases, respiration of an atmosphere of compressed air has been given with marked success. With the object of increasing excretion, dry cupping, over the kidneys, is often useful.

The action of the skin should be maintained as much as possible, for there is a very close connection between the kidneys and the cutaneous surface. Extensive burns, or skin eruptions, are often associated with albuminuria. A rabbit, shaved and varnished, quickly dies

comatose. Death, which is preceded by great fall in the temperature, is no doubt due to the action of some poisonous product which is retained in the system. When the cutaneous surface is cold, perspiration is diminished, and the kidney excretes an increased amount of water, and urinary solids. It so attempts to compensate for the diminished functional activity of the skin. To a slight extent the converse of this is true; an increase of the cutaneous functions assists renal excretion. In uræmia, urea is occasionally noticed as a glistening powder upon the skin, and certain cutaneous eruptions sometimes arise, some of which are probably due to the presence of irritating excrementitious substances in the perspiration ; urea, uric acid, blood, albumen, oxalate of lime, indigo, bilirubin, and other pigments, as well as lactic acid and sugar, have all been detected in the sweat of certain pathological conditions. The total amount of poisonous material excreted in this manner, is, however, small. Besides the benefit which results from increasing this excretion, the production of diaphoresis is advisable on account of the lowering of the blood pressure which accompanies it. To induce perspiration, drugs or baths may be employed. The drug most commonly used is pilocarpine nitrate, it is most reliable when administered hypodermically, and when it is supplemented by warmth to the surface. The centres of the salivary and sweat glands are stimulated, as well as the peripheral termination of their nerves. It does not appear to increase the secretion of bile. The action of pilocarpine has to be carefully watched as it sometimes causes great depression of the heart : for this reason Fordyce Barker considers it a dangerous drug,

discretion in its use is very necessary where cardiac failure is a feature of the disease. Atropine antagonises its action completely, and should be kept at hand in cases of sudden collapse. Hot air, or vapour, baths, are a favourite means of procuring the action of the skin, and they may be employed to aid the effects of pilocarpine, or used separately, when the drug is contraindicated. Occasionally a warm bath seems to induce an attack of uræmia in patients suffering from renal disease, and who have previously exhibited no sign of its onset. The cause of this unfortunate result appears to be the increased amount of poisonous material which circulates through the brain by reason of the dilatation of the cerebral vessels.

It was at one time thought that the intestinal tract could be made to assume, in a great measure, the excretion of urinary substances ; this is in part, no doubt, true, but as Bouchard has shewn, it is not wise to do too much with hydragogue purgatives, for although water is removed, causing a diminution of œdema and serous effusion, and also carrying away a portion of the toxic material, yet the result is a concentration of poisonous substance, and the kidney also loses its most powerful inducement to excretion. Venesection is a very efficient means of diminishing the amount of the extractives, and arterial tension. The benefit which follows its employment is often startling but frequently temporary. A bleeding of one ounce removes as much of the extractives as nine ounces of liquid diarrhœa, or 16 gallons of perspiration. (Bouchard.) Venesection is especially useful in those cases of uræmia which depend upon acute or temporary causes, such as scarlatinal nephritis,

or puerperal eclampsia. Children, the aged, and cases of great debility, do not form good subjects for venesection. Usually, the presence of cyanosis, strongly pulsating carotids, and deep coma, with suffusion of the face, are indications for immediate blood-letting.

SPECIAL TREATMENT.

This must always be accompanied by adherence to the principles laid down under the heading of general treatment, and especially of that which is directed at intestinal asepsis.

Headache often seems to depend upon high arterial pressure, and an attempt should be made to bring about its reduction. A smart purge is one of the best methods of accomplishing this; pulvis jalapæ co. is a useful drug for this purpose, and the treatment may be continued by an occasional dose of nitro-glycerine ♏j or ij, of a one per cent. solution in rectified spirit, given in a little water, or amyl nitrite may be prescribed thus :—

℞ Amyl Nitrit. ♏xvj } *misce et* | Pulv. Tragac. - gr. iv
Spirit. Rect. ʒij } *adde* | Aq. distil. - ad ʒiv

One teaspoonful every four hours.

A noticeable result from the exhibition of amyl nitrite is the large increase of uric acid in the urine.

Caffeine citrate, gr. iv, is often serviceable, and may be given with or without quinine.

Uræmic blindness, deafness, and perversions of general sensation, demand hot air baths and sharp purgation.

Vomiting and diarrhœa, unless excessive, should not be checked, as these no doubt are some of the means nature chooses to adopt for her own protection. If the

vomiting be very severe, milk and soda water, iced if necessary, will probably be retained; small doses of morphia are useful in lessening the excitability of the stomach, and reducing diarrhœa.

Gastric catarrh calls for a very careful selection of the diet; raw vegetables, sweets, uncooked fruits, or fatty foods should be discarded, and relief may be obtained by administration of bismuth and soda mixtures, or other gastric sedatives.

Uræmic asthma. Numerous remedies have been recommended for this distressing symptom, but it cannot be said that any unfailingly reliable have yet been found. Carter states that he has seen benefit follow the administration of ozonic ether in doses of one drachm. Delafield recommends reduction of the blood pressure, and opium, which Carter says is specially indicated when there is dilatation of the pupil. Oxygen inhalations have not in my experience been followed by more than temporary relief. Amyl- or ethyl-nitrite are also occasionally useful in the treatment of this symptom.

For œdema of the glottis, ice may be sucked; puncture, tracheotomy, or intubation, may be practised in severer cases, but are of no service when œdema of the lungs co-exists, and is extensive. The action of the skin and kidneys must be secured at all hazards in this condition.

Cardiac symptoms require rest in bed, and to be treated with heart tonics, digitalis, strophanthus, caffeine, etc., whilst attempts may be made to reduce peripheral resistance by the exhibition of vascular dilators, such as the nitrites. In these cases active purgation is especially to be avoided on account of the risk of inducing cardiac failure.

Coma and hemiplegia will require in appropriate cases, described under General Treatment, venesection and hot air baths; usually, too, sharp purgation is beneficial. It is said that improvement sometimes follows a dilution of the blood by means of normal saline solutions, but I have no experience of this treatment.

Richardière (*Union Méd.*, December 5th, 1896) has used large injections of artificial serum in two cases with good results. His practice is to bleed to 300 to 400 grammes, and immediately inject slowly into the cellular tissue 800 grammes of the serum at the temperature of the body. The serum is made after Hayem's formula, and is used aseptically. His first case presented intense dyspnœa, numerous mucous and subcrepitant *râles* all over the chest, and nearly all the subjective symptoms of Bright's disease, with extensive œdema. Under ordinary treatment the patient got worse, respirations rising to 48 per minute, with Cheyne-Stokes character, and suffered from hallucinations, so that six days after admission he was comatose, and dyspnœa was still increasing. Bleeding to 300 grammes, with injection immediately after, was followed by a fall of pulse-rate from 140 to 120: the temperature rose from 37·8° to 37·9°, and the respiration became slower and regular. During the next few days the urine increased in amount, then fell again, when Cheyne-Stokes breathing reappeared, and the state became alarming. The patient was bled again 250 grammes, and injected 800 grammes; a second injection was given six hours afterwards. Temperature rose from 35·8° to 37°, and no further trouble occurred, although the œdema persisted; respirations remaining regular, and he remained free from somnolence, passing about 1 litre of

urine in twenty-four hours. The second case presented signs of grave uræmia; injection was followed by improvement, which failed again in twenty hours. A second injection was followed by profuse diarrhœa, and caused permanent amelioration of the condition. He quotes other cases, and points out that the injection is harmless, though painful; it raises the temperature, slows the pulse, and steadies breathing previously irregular, and of the Cheyne-Stokes character, lessening the rate at the same time. It also increases the amount of urine, and seems to have a tendency to produce diarrhœa, which he looks on as favourable.

In prolonged and feeble cases, it may be advisable to administer peptonised milk per rectum.

Convulsions. The treatment of convulsions occurring in uræmia, not associated with pregnancy, calls for immediate attention. Frequently the attack is so slight that the convulsion has taken place before anything can be done, and it may not recur. In the more severe variety where convulsions follow one another very quickly, and give rise to a condition resembling the status epilepticus, energetic measures must be adopted. Care must be taken that the tongue be not bitten. A piece of wood, surrounded by flannel, and placed between the teeth, is a ready means of preventing this. Attention must be paid that respiration is unimpeded. Purgation should be secured by the administration of calomel and croton oil, which may be mixed in a little butter, and placed far back on the tongue of those patients who are unable to swallow. The violence of the convulsions can be controlled by inhalations of chloroform, and the administration of chloral per rectum, every four

hours, is very useful to continue its effect. Morphia hypodermically is recommended, and is occasionally of service. Bromide of sodium, or ammonium, are often very useful, but the potassium salts should be avoided. The skin must be induced to act freely, as directed under general treatment. In young adults in whom there is strong pulsation of the carotids, cyanosis, and congestion, venesection is often of much service.

PUERPERAL ECLAMPSIA.—Slight cases of puerperal eclampsia, with no subsequent coma occurring before the full term of pregnancy, may be treated in the same manner as uræmic convulsions when not so connected. (Galabin.) Cases of greater severity, or when occurring at the completion of pregnancy, shew certain special indications. Opinion was formerly much divided as to the advisability of interfering with the course of pregnancy. It was taught that convulsions were to be alone attended to, and that the labour might be allowed to look after itself. (Gooch.) Shroeder advised that no interference with the uterus, or its contents, should be practised, and this for the safety of the mother. The most that should be done when the life of the child is in danger, is that labour might be hastened to secure an early delivery. Now the maxim is, in severe cases, that if labour has not commenced it should be induced by puncturing the membranes. Sometimes this operation stops the fits, and labour proceeds naturally. Chloroform narcosis should always be used during any manipulation which may be necessary. If dilatation of the cervix be delayed, it may be artificially assisted by means of hydrostatic dilators, and then if the fits continue and labour be protracted, an application of the forceps should

be made, as soon as practicable, or version practised and delivery effected. Craniotomy is sometimes advisable when there is undoubted evidence of the death of the child. Playfair, on the other hand, is very emphatic as to the correct mode of procedure when labour has not begun. He maintains that no active measures should be taken to induce it, even vaginal examinations may give rise to a fresh outburst of convulsions. "The membranes can, however, be ruptured with advantage, as this is a procedure which gives rise to very little irritation. Forcible dilatation of the os, and especially version, are strongly contra-indicated." Tyler Smith's old advice seems the most reasonable. He says, if the fits appear to be evidently induced or kept up by the pressure of the fœtus, and the head be within reach, then the forceps, or even craniotomy may be resorted to; but, if the operation is likely to prove a greater source of irritation than leaving the case to nature, no interference should be made.

Chloral, or hypodermic injections of morphia, will probably cause any uræmic convulsions, which may continue after delivery, to abate. Inhalations of chloroform may occasionally be necessary should they persist; usually, however, after delivery has been effected, all symptoms of eclampsia quickly disappear, without further treatment, and even albuminuria becomes much diminished, and may entirely vanish.

BIBLIOGRAPHY.

BOUCHARD. Leçons sur les autointoxication dans les maladies.

———— Poisons de l'organisme et toxicité urinaire.

BRUNTON, LAUDER. Pathology of Dropsy. "Practitioner," Vol. xxxi.

CARTER, W. Bradshawe Lecture, 1888.

DICKINSON. On the pathology and treatment of Albuminuria.

FELTZ & RITTER. De l'urémie experimentale.

GAUTIER. Sur les ptomaines de progrés Medical.

HAIG. Uric Acid Diathesis.

LANDOIS & STIRLING. Text-book of Physiology.

LEPINE ET AUBERT. Contributions a l'étude de la secrétion urinaire.

LLOYD-JONES. Blood changes met with in Renal Disease. "Practitioner," Vol. xliii.

MACMUNN. Researches into the colouring matter of urine.

MAHOMED. Some clinical aspects of Bright's Disease.

MILLARD. Bright's Disease of the Kidneys.

NIEMEYER. Text-book of Medicine.

PEABODY. The relation existing between retention of urea and uræmia. "New York Medical Records," Vol. xvii.

RALFE. A practical treatise on Diseases of the Kidneys and Urinary Derangements.

ROBERTS. A practical treatise on Urinary and Renal Diseases.

ROSENSTEIN. Die Pathologie und Therapie der Nieren Krankheiten.

SAUNDBY. Bright's Disease.

SNYERS. Pathologie des Nephrites chroniques.

STEWART, GRAINGER. Treatment of Bright's Diseasc. "Lancet," 1893, p. 99.

TWENTIETH CENTURY OF MEDICINE. Article "Urinary Diseases."

APPENDIX.

CLINICAL NOTES OF THE SALIENT FEATURES OF SOME ILLUSTRATIVE CASES OF URÆMIA OCCURRING IN BRIGHT'S DISEASE.

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CLINICAL NOTES OF THE SALIENT FEATURES OF SOME ILLUSTRATIVE CASES OF URÆMIA OCCURRING IN BRIGHT'S DISEASE.

CASE 1. *Urœmia occurring in the course of Acute Nephritis; Temporary Blindness; Recovery.*—William J——, aged 10, schoolboy, came under treatment for œdema of the feet and ankles, and face, and also persistent headache, March 4th, 1894.

Previous History.—His mother states that ten days ago he was in good health. Twelve months previously he had diphtheria, and this, with the exception of a slight attack of measles which he had when an infant, is the only complaint he has suffered from. There was no œdema either during or after the diphtheria.

Condition upon Examination.—The patient is an undersized boy, rather anæmic but well-nourished. There is much swelling of the face and œdema of the ankles, and also of the lower part of the abdomen; there is no ascites. Temperature normal, tongue furred, appetite poor, he is sometimes sick in the mornings. Bowels constipated. Lungs normal, respirations 20. Heart's apex displaced downwards and outwards, being half an inch outside the nipple-line. There is a mitral systolic murmur and re-duplication of the second sound. Pulse 84—regular, small, but hardish. Has had frequent epistaxis. Liver and spleen normal. Urine 22 oz.. sp. gr. 1022, acid, dark coloured, deposits blood-cells, epithelial, hyaline, and granular casts; urea 1·5 per cent., albumen $\frac{1}{4}$, sugar absent. The pupils are equal and regular, react well to light and distance; ophthalmoscopically only slight œdema is discernible. There is some deafness on the left side, which is, however, due to changes in the middle ear.

Treatment.—The patient was put to bed, ordered a mild aperient and

℞ Liq. Ammon. Acet.	℥xl	Sp. Ætheris Nit.	℥x
Tr. Digitalis	℥iij	Aq. Menth. Pip.	ʒiv

To be taken every three hours.

A diet of milk and soda water and Benger's food was instructed to be given, and a bath at 100°F., in which the child was to be immersed to the chin and allowed to remain a

quarter of an hour, the temperature of the bath being maintained. He was then to be wrapped in a warm sheet and put to bed, with a hot bottle. The bath and aperient were to be repeated each day.

A week after this treatment had been adhered to, there was much less œdema of the face and extremities. The condition of the urine was not quite so satisfactory, amounting to 24 oz. per twenty-four hours, sp. gr. 1016; albumen about the same as before, but the urea was reduced to 1·25 per cent., 135 grains per diem. The next day, the nurse said he had been complaining greatly of headache, and when asleep continually ground his teeth, and the legs twitched. He has been sick again this morning. The bowels have acted regularly each day; a grain of jalapin was ordered, and the bath morning and night. The food was restricted to milk and soda-water. He was seen later the same day, the bowels had acted twice, motions offensive, his head-ache was very troublesome, which he now said extended all over the head; has been sick once since morning. He has hardly passed any urine all day, what he has is very dark, from blood, and clouded; large number of casts are present, albumen nearly one-half; urea 1·25 per cent.

He was ordered

℞ Chloral. Hydrat. | Sodii Bromid. āā gr. x

to be followed by hourly doses of Benzonaphthol gr. iv. in cachets. The first part of the night he slept well, but awoke at 3 a.m. and had three slight convulsions, which affected chiefly the face and upper part of the body; these were followed by drowsiness. A dose of the chloral hydr. mixture was given per rectum, after which he again slept; no further convulsions occurred, and upon waking he passed a large quantity of water. On the following day the patient seemed better, he had no headache or pain of any sort, there was less œdema. Upon examining the retinæ ophthalmoscopically, they seemed, with the exception of a slight œdema, to be normal in appearance, but there was total blindness of the left eye and some dulness of vision in the right. Urine 30 oz. sp. gr. 1018, acid, dark coloured; albumen ¼, urea 1·75 per cent.; temp. 99·0F.; pulse 80.

℞ Benzonaphthol gr. iv | Bismuth Salicyl. gr. iij

Ordered to be given every two hours, and a dose of the Chloral Hyd. mixture at night time. Milk diet continued.

From this point all symptoms of uræmia disappeared, the blindness slowly gave way, but a week after there was still considerable weakness in the left eye, but which finally recovered. At the end of a month all the œdema had disappeared, there was no sickness or headache. Temperature normal, respirations 18, pulse softer, easily compressible, 76 per minute. Urine 34 oz. acid, slight deposit, few casts, albumen about a tenth, urea 2 per cent., no blood by the guaiacum and ozonic ether test. The sight was now quite good, no difference between the eyes was observable. The benzonaphthol and bismuth salicylate which had been gradually reduced, was now finally stopped. Fish and fowl added to the diet, but the warm bath was continued. When last heard of a year after the previous note, he was quite well, no return of the symptoms had taken place.

CASE 2.* *Uræmic Convulsions occurring in the course of Scarlatinal Nephritis; Athermia; Death.*—Jane D——, aged 8, suffering from scarlatina, headache, and œdema, October 25th, 1890.

Previous History.—Until the present illness the patient has been strong and healthy, had no other infectious complaint. Scarlatinal symptoms showed themselves ten days ago; rash was not well marked, no great constitutional disturbance; case promised to be a mild one. Throughout the attack, an exclusively milk diet has been taken, and there has been no albuminuria until two days ago.

Present Condition.—She is a well nourished child, pale-faced. Œdema under the eyes; considerable œdema of the legs and lower part of the body. Temp. 98·2F. Tongue furred, appetite bad, has vomited several times, constipated, liver normal, spleen enlarged. Heart's apex beats in the fifth space about half an inch outside nipple line. Action forcible, irregular, reduplication of the second sound at the base. Pulse irregular, hardish, and small, 105. Breath-sounds feeble, slight dulness at both bases. Occasional moist *râle*. Resp. 22, urine 14 oz., acid, sp. gr. 1022; deposit of urates, granular and hyaline casts, considerable quantity of blood, albumen $\frac{3}{4}$, urea 110 grs.

* For permission to make notes upon this case I am indebted to Dr. Newman.

Pupils contracted, retinæ seem normal. Desquamation is well advanced, throat still very red, tonsils and uvula swollen.

Treatment.—Warm bath night and morning, temp. 100°, in which she is to remain twenty minutes. Jalapine gr. j, and

℞	Tr. Digit.	℥j	Glycerine	℥j
	Liq. Ammon. Acet.	℥jss	Aq. ad	℥viij
	Sp. Ætheris Nit.	℥iv		

Two teaspoonfuls every three hours.'

Diet restricted to milk and barley-water or whey, which is taken readily.

October 26th.—Has passed a very restless night; has been sick once this morning (curdled milk, trace of urea). Skin harsh and dry, œdema is no less. Bowels acted twice, watery motion with scybala; urine, some lost in bed, the remainder 12 oz. acid, dark coloured, sp. gr. 1025. Albumen ¾, blood and casts as before, urea in the 12 oz. 96 grains; temp. 97·2°. Ordered, warm wet pack, and pilocarpine gr. ⅛, hypodermically.

October 27th.—Has had a better night, perspired freely, not been sick. Jalapine gr. j repeated. Temp. 97·4°, pulse 102. Urine 13 oz., sp. gr. 1024, acid; albumen ⅝, blood and casts, urea 102 grains; copious deposit, dark coloured.

October 28th.—Complains greatly of headache, sick twice, pupils contracted, retinæ again examined, haziness, especially in the right eye. Œdema seems more pronounced, face much swollen, lower part of abdomen and ankles likewise. Temp. 97·0, pulse 106; urine 14 oz., sp. gr. 1026, acid; albumen ¾ blood, casts, etc.; urea 98 grains. Ordered (for the relief of headache) caffeinæ cit. gr. ij, jalapine gr. j, dry cupping over loins.

October 29th, 5 a.m.—Has been sick twice in the night, when it was noticed the skin was very cold; the temperature in the rectum was 95·6; warm pack given at 6 a.m. Temperature taken again after a few minutes registered 95·4F.; at 6·45 had a slight convulsion, succeeded in a few minutes by two others of greater severity; consciousness was lost in the two latter. 7.15 a.m.—She died collapsed; no urine was passed since last evening at 5 o'clock. As the case occurred in private practice, no autopsy was requested.

Case 3. *Puerperal Eclampsia, occurring during the ninth month of Pregnancy. Induction of labour; Recovery.*—Mary

S——, aged 24, complained of headache, attacks of giddiness and sleeplessness, Jan. 14th, 1894.

Previous History.—The patient always had fair health, no history of scarlatina, or any other infectious complaint. Married at 22; has one child; no trouble at that confinement; believes she has now just entered the ninth month of pregnancy. Present symptoms of about three weeks' duration, they vary in intensity. Has been much constipated the last few months.

Condition upon Examination.—She was anæmic, complexion pasty, slight puffiness below the eyes; some œdema about the ankles, was well nourished, tongue coated, and breath objectionable. Area of cardiac dulness increased, no murmurs, accentuation of the second sound at the base. Slight varicosity of left saphenous vein, pulse 72, high tension, incompressible. Lungs normal, R 25. She was formerly of a cheerful temperament, but has lately become nervous and irritable. Pupils small, equal react to light and distance, retinæ normal. Slight numbness in the toes of the left foot. Urine 85 oz., sp. gr. 1015, acid, clouded by urates. Albumen, $\frac{1}{6}$; urea, 1.5 per cent.; hyaline granular casts; no sugar.

Treatment.—Patient directed to remain in bed; fish, chicken, and milk, substituted for ordinary diet. Calomel, gr. iij, to be taken at night, saline purge in the morning.

By noon next day her headache had gone. She no longer felt giddy. Bowels acted three times without pain.

Jan. 18th, contrary to instructions, she came downstairs. The same evening convulsions commenced quite suddenly, beginning on the left side, and rapidly becoming general. Consciousness was quite lost; foaming at the mouth, grinding of the teeth.

The convulsions lasted about three minutes, succeeded by stupor. Calomel gr. iij, croton oil min. j, were given, and a rectal injection of chloral, gr. xx. After an interval of four hours, during which time the bowels moved once, three convulsions, exactly like the first, occurred, with a space of only three or four minutes between each. These were succeeded by coma. Pupils widely dilated, insensitive to light. Temp. 100 F. Occasional twitching of left hand. Further injection of chloral, gr. xx, given.

This condition lasted for an hour, when the fits returned

with severity; inhalations of chloroform were commenced, and pushed whenever a convulsion seemed likely to occur. Morphine acetate, gr. $\frac{1}{3}$, was given hypodermically, but although the fits were, doubtless, restrained by these measures, they shewed no signs of entirely disappearing. It was decided to induce premature labour. Chloroform narcosis being obtained the membranes were ruptured. Labour, however, did not commence, and the fits continued; the os was then dilated by hydrostatic dilators and the forceps applied. The child, a male, when born, seemed dead, but revived after prolonged artificial respiration and alternate hot and cold baths. After the removal of the placenta only two convulsions occurred, the patient passed into a deep sleep, from which she at length awoke, and complained only of violent headache, which soon passed off. Memory of events occurring the day preceding the convulsions was quite wanting, but returned in the course of a few days.

The first urine passed on returning to consciousness, contained fully one-half volume albumen; in the following twenty-four hours urea amounted 650 grains. At the end of a month albumen was recognisable as only a trace, casts being entirely absent.

Case 4. *Cheyne-Stokes respiration, uræmic hiccough in chronic Bright's Disease; Recovery.*—Richard J——, aged 40, engineer, complains of dropsy, shortness of breath, and headache, June 25th, 1893.

Previous History.—The patient has always been considered delicate, has had scarlatina, and rheumatic fever, at the ages of 15 and 19 respectively. Drinks large quantity of beer, but is seldom "the worse for it." Remembers his feet were swollen after the scarlatina, but until about a month ago, when the present symptoms commenced, they were not swollen. He has been sick two or three times lately.

Condition upon Examination.—He is a pale pasty-faced man, well nourished and developed. Slight œdema about eyes, feet, and ankles, lower part of abdomen; no ascites. Temp. 97·8. Lungs over-distended, emphysematous, breath sounds feeble, inspiration prolonged, occasional *râle*, bronchial breathing absent, Resp. 28. Respiration is much laboured, speaks in gasps. Sometimes he breathes comfortably for days;

dyspnœa comes on especially after exertion, attacks are becoming more frequent.

Heart's apex inside nipple line, sixth interspace impulse heaving, action irregular. Loud mitral systolic rough murmur, aortic second sound clear, sharp, and accentuated, tricuspid systolic bruit. Pulse hard, high tension, irregular, P. 72. Eyes normal, pupils dilated, sensitive to light. Reflexes normal. Headache occipital, worse when lying down. Tinnitus occasionally, sensations normal.

Urine, 63 oz.; acid, sp. gr. 1012. Urea, one per cent.; albumen, ½ volume; blood, a trace; granular, fatty, hyaline casts with blood cells.

Tongue furred, indented, bowels constipated, vomited this morning when getting up.

Treatment.—Ordered to remain in bed; diet of milk, and farinaceous foods, no meat. All stimulants forbidden. Hot-air bath to be given daily. Bowels to be freely moved by magnes. sulph. each morning :—

℞ Pulv. Digit. - - gr. j | Pil. Hydrarg. - - - gr. iss
Pulv. Scillæ - gr. iss |

Fiat Pil. One to be taken three times a day.

June 28th.—Seems to be going on well. Urine, 60 oz.; acid, sp. gr. 1015; urea, 1·2 per cent.; albumen, ⅓.

July 3rd.—Has vomited curdled milk after breakfast; about an hour later hiccough commenced; obliges him to sit up. Urine, 67 oz.; acid, sp. gr. 1014; albumen, ⅓; urea not estimated; granular casts and blood cells as when first seen.

Ordered ice to suck, soda water and milk, and

Ac. Hydrocy. dil. - - ♏iij | Aq. ad. - - - - ℥j
Sp. Chlorof. - - - ♏xv |

Every four hours.

July 6th.—Numerous remedies have been tried to check the hiccough, but no benefit was derived from any of them. The hiccough stopped abruptly last night. He is very short-winded now, but says that whilst the hiccough lasted he breathed comfortably. There is no change in the condition of the lungs to account for the increased dyspnœa. Heart is acting fairly well. Pulse more regular than when first examined, 80 to the minute.

Pupils are much smaller. There is no headache. Urine,

60 oz.; acid, sp. gr. 1015; albumen, $\frac{1}{3}$; urea, 1·2 per cent.; blood cells and casts as before.

July 8th.—At 3 a.m. this morning Cheyne-Stokes breathing commenced. At first the interval of no respiration was only short, but gradually lengthened, and averaged, at its worst, 16 seconds: continuous respiration took place for about 40 seconds, during which time pulse rate was increased, amounting to 96 per minute—during the pause the rate was much reduced, and towards its end was only 60 per minute—whole attack Cheyne-Stokes breathing lasted for two hours, gradually passing off, and succeeded by ordinary dyspnœa. Amyl-nitrite, ♏ij, one per cent. solution was administered with two oz. of whiskey.

July 9th.—Patient had a return of Cheyne-Stokes breathing last night, occurring at intervals of four hours. Pupils were very contracted, meantime amyl-nitrite was given as before, but did not afford much relief. Tinct. belladonna, ♏xv, in an oz. of whiskey and water was followed by disappearance of symptoms, and after a second dose dilatation of the pupil.

Ordered:—

℞ Tinct. Digit. - -	♏v	Sp. Junip. - - -	♏xxx
Tinct. Bellad. - -	♏v	Inf. Scoparii ad - -	- ℥j
Sp. Ætheris Nit. -	ʒss		

Fiat Mist. Two tablespoonfuls four times a day.

July 16th.—Has had no further attack of Cheyne-Stokes respiration, dyspnœa has not been so troublesome. Hiccough returned for about half-an-hour this morning, but has disappeared again. Urine, 56 oz.; acid, sp. gr. 1012; urea, 1.6 per cent.; albumen, $\frac{1}{4}$; blood a trace, granular, fatty, and hyaline casts. After this date, with the exception of occasional headache no uræmic symptom appeared. When last heard of, November 25th, he was going about his work as usual, and expressed himself as being cured.

Case 5. *Uræmic Coma, occurring in Chronic Renal Disease; Recovery.*—William B——, aged 47, complained of swelling in the feet and ankles, and headache, Nov. 12th, 1895.

Previous History.—Has always had good health, no history of scarlatina; his father was gouty, but he himself has shown no symptoms of gout. For some time he has been obliged to get up at night several times to pass water. He is not a tee-totaler, but strictly temperate, drinks no spirits.

Condition upon Examination.—He is a stout muscular man, somewhat anæmic, considerable œdema about the feet and ankle, T. 98·2 F.

Tongue clean; appetite fair; slight uneasiness after food; bowels slightly constipated, liver and spleen normal. Heart's apex lies just outside the nipple line in the fifth interspace; soft systolic murmur at apex, accentuation of the second sound, P. 90. Lungs, resonance normal, signs of slight congestion in the bases. R. 22. Pupils contracted, react slowly to light, says he does not see as clearly as formerly. Ophthalmoscopically there are seen to be, in both retinæ, numerous atrophic patches and œdema.

Urine, 40 oz., yellow, and slightly smoky; small whitish deposit, acid; sp. gr., 1017; albumen, $\frac{3}{4}$; urea, 1·2 per cent.; hyaline, granular, and epithelial casts, white and red blood corpuscles.

Treatment.—Ordered to remain in bed, milk and fish diet, and Pulvis Jalapæ Co. gr. xl, and

℞ Liq. Ammon. Acet. ʒij | Sp. Ætheris Nit. ♏xl
Tr. Digit. ♏viij | Inf. Scoparii ad ʒj
Four times a day.

A week later there was some diminution in the amount of the œdema, headache still continued, situated chiefly in the occipital region, has been much troubled by subjective ocular symptoms, black spots.

Urine, 45 oz., acid, sp. gr. 1016; urea, ·9 per cent.; albumen, $\frac{5}{8}$; trace of blood casts as before.

Ordered warm baths twice a day. Benzonaphthol, gr. x, in cachet, and following pill:—

℞ Pil. Hydrarg. - - gr. iss | Pulv. Digit. - - - gr. ss
Pulv. Scillæ - - gr. iss |
Fiat. Pil. One pill to be taken three times a day.

During the following week the volume of urine increased to a maximum of 55 oz. Albumen varied from $\frac{1}{2}$ to $\frac{7}{8}$; urea, from ·75 per cent. to 1·2 per cent. Towards the end of the week he began to be drowsy and apathetic, tongue became dry, and sordes formed on the teeth. He vomited several times. Pupils reacted only very slowly to light, it was difficult to arouse him to take his food, he commenced to talk in an incoherent manner, and became very restless.

These symptoms increased until it was impossible to arouse

him at all. Evacuation of the bowels and urine took place unconsciously.

Ordered hot-air bath, pilocarpine-nitrate gr. $\frac{1}{3}$, hypodermically. This produced copious perspiration. A good action of the bowels was obtained by calomel, gr. v., after which he slowly returned to consciousness, and continued to improve until a month later. When last seen he was comparatively well. Some œdema about the ankles was still present, much less than formerly; he had no headache.

Urine, 52 oz. per diem; albumen, $\frac{1}{4}$; no blood; urea, 1·4 per cent.; hyaline and granular casts still present, but in a much smaller number than before.

CASE 6. *Uræmia occurring in a case of Granular Contracted Kidney. Asthma; Coma; Death.*—John J——, aged 56, seaman, complained of difficulty of breathing and dropsy, Oct. 26th, 1892.

Previous History.—Patient has always been a temperate man, had rheumatic fever when he was 20. Small-pox some years ago, age not known. No family history of gout or other hereditary disease.

Condition upon Examination.—He is a tall, thin, anæmic man; there is some swelling of the feet and ankles, and upon the back of the hands; the present symptoms date from a month ago. T. 98·6.

Tongue furred, appetite fair, vomits occasionally irrespective of taking food, after which there is sometimes epigastric pain; bowels constipated. Heart's action forcible, apex beats one inch outside nipple line in the sixth interspace; systolic murmur at apex; accentuation of the second sound at the base; larger blood vessels atheromatous, P. 90, hard and incompressible, sphygmogram shews high tension in a typical manner. Posteriorly, on the left side of the chest, usual signs of effusion extending to the angle of the scapula. Breath sounds feeble, occasional *râles*. On the right side but little fluid. Breath sounds normal. R. 25. Urine, 35 oz., acid, sp. gr. 1014; albumen, $\frac{1}{2}$; urea, 260 grs.; cloudy, small deposit, a few granular and hyaline casts; has been obliged to get up three or four times each night to pass water, but lately this symptom has not been so troublesome.

Suffers from headache, and dimness of vision. Arcus

senilis fairly well marked. Pupils contracted, react slowly to light and distance. Examination of the retinæ is difficult as the patient objects to the pupils being dilated. As far as can be made out retinitis is not present.

Treatment.—The patient sent to bed, left pleura tapped, 96 oz. serous fluid drawn off, after which breathing became easier. A sleep of several hours followed. Fish, chicken, and milk, were ordered, and medicinally :—

℞ Pil. Hydrarg.		Pulv. Digit. - - -	gr. ss
Pulv. Scillæ -	āā gr. iss		

One pill to be taken three times a day.

Oct. 27th.—He had a bad attack of asthma, evidently uræmic. T. 97·2. Bowels have acted twice during the day. Urine, 40 oz., acid, sp. gr. 1015 ; albumen, $\frac{1}{3}$; urea, 270. Ordered

Ozonic Æther, ℥j, in Liq. Ammon. Acet. ℥iv.

every two hours. No benefit resulted. Numerous other remedies were tried ; inhalations of a few drops of chloroform seemed to afford the most relief.

The attack lasted about six hours, upon its passing off, naphthalin, gr. x, in cachet, every three hours was given.

Nov. 4th.—During the last week he has had slight return of dyspnœa which seemed to be controlled by tinc. of belladonna, min. 10, every two hours. It was noticed that dilatation of the pupil, which was very small at the commencement of an attack, coincided with the relief of the dyspnœa.

His general condition is much the same. More water, however, is passed, from 50 to 60 oz. per diem. Urine, dark-coloured (from naphthalin), albumen, $\frac{1}{3}$, sp. gr. 1014 ; urea, 300 grs.

P. 100, tense, irregular; occasionally intermits, 84 per minute; no re-accumulation of fluid in the pleura; breath sounds feeble posteriorly; resp 22. It is impossible to continue the naphthalin on account of the sickness which it causes. Ordered the following mixture every three hours:

℞ Caffeinæ Cit.	gr. v	Inf. Digit.	℥ij
Sod. benzo.	gr. xv	Aq. ad	℥j
Sp. Junip.	♏xx		

For the next six days the urine was increased, amounting to 55 oz., 60 oz., 72 oz., 67 oz., 59 oz., and 55 oz.; albumen

varied from $\frac{1}{8}$ to $\frac{1}{4}$, sp. gr., 1010 to 1016; urea, 206 to 310 grs. per diem.

Nov. 11th.—The seventh day, he seemed worse; complained greatly of headache; considerably more œdema about the feet and ankles, also some beneath the eyes; temp. 97·0 F; no fluid in chest; breathing shallow and hurried; dyspnœa was not complained of; R. 28; heart's action irregular; mitral systolic murmur very distinct; P. 96, more tense; urine only 30 oz., acid, sp. gr. 1022, clouded, blood; albumen, $\frac{3}{4}$; urea, 260 grs.; increased number of granular and hyaline casts.

Ordered: Dry cupping over the kidneys; hot-air bath, and Pulvis Jalapæ Co. ʒj; copious perspiration followed; the bowels were well moved once.

Six hours later the breathing became more difficult, and the patient was comatosed.

Pupils pin-point, divergent; tongue furred; lips dry; has vomited once.

Respiration stertorous, noisy; R. 28; temp. 96·2 F.

Pulse 100, irregular, occasionally intermittent; urine passed in the bed.

Skin acting well; perspiring freely.

It was decided to try the effect of venesection. After 6 oz. had been withdrawn, he shewed signs of returning consciousness; bleeding was then stopped; he could now be aroused for an instant by shouting; remained in the same condition for three hours; died at 7.25 a.m.

No autopsy could be obtained.

Case 7. *Mania occurring with temporary Albuminuria in an insane patient.*—Eliza S——, aged 36, complains of occipital headache and noises in the ears. February 14th, 1891.

Previous History.—There is nothing in the family history of importance. So far as known patient has had no infectious disease, but has always been considered delicate. Married at 23; has two children, aged 10 and 6. Three weeks after birth of second she became despondent and heard voices, was then sent to an asylum, where she remained 18 months; was discharged as recovered. Friends say she is generally despondent and grumbling at trivialities. These attacks become worse during menstruation; occasionally she is much more cheerful.

For the last three months she has been very gloomy, sometimes not speaking for days together.

Condition upon Examination.—Patient is a medium-sized woman—plethoric, and well nourished; complexion disfigured by acne; no œdema. Temp. 97·4F. Tongue thickly coated, mouth dry, teeth defective, suffers pain after food, very constipated, appetite capricious, cardiac action feeble, irregular, occasionally intermits; heart-sounds distinct, blowing systolic murmur mitral area; apex beat fifth interspace half an inch within nipple line. Pulse soft, compressible, irregular, intermittent 70.

Lungs normal, liver and spleen normal. Urine 42 oz., acid, dark-coloured; sp. gr. 1022, copious deposit of urates, urea not estimated. Albumen none, hyaline and granular casts none, no blood or sugar. Pupils dilated, react slowly to light, plantar reflex absent, deep reflexes normal.

Mental Condition.—Is very slow in replying to questions, evidently on her guard; admits she does not sleep well at night on account of the rats overhead (there are no rats in the house). Fancies her child is bitten by rats at night, explains that these are not delusions; says her husband is always calling to her by name. Her husband says she is in great dread of being sent back to an asylum, and she frequently refuses food with disgust after taking a mouthful or two.

Treatment.—Ordered calomel gr. v, to be followed by a seidlitz powder and quinine tonics.

February 21st.—Seems better mentally, has taken the calomel twice during the week, each dose being followed by a copious evacuation of the bowels. Is taking her meals better, and is more cheerful and talkative. Instructed to keep her bowels open by means of colocynth and hyoscyamus pills, and to take regular exercise; tonic to be continued.

March 30th.—Since last note, patient continued to improve until two days ago, when she became morose, suspicious, refused her food, and was very quarrelsome. Physically she is in much the same condition as when first seen. No examination of the urine was made to-day. Bowels are again very constipated, as lately no purgative has been taken. A large soap and water enema brought away many scybalatous masses. Croton oil ♏j was given by the mouth.

March 31st.—Patient had an altercation last night with her

husband, which ended in her becoming very excited and hysterical. This morning she is quite incoherent, constantly moving about, and using offensive language. Attention was called to the small amount of urine passed during the night. An examination of this shewed it to contain ⅓ of albumen by volume. This precipitate was also obtained by boiling. There were a few hyaline and epithelial casts, no blood or sugar. Urea 1·4 per cent., sp. gr. 1022. Ordered croton oil ♏j, and chloral hyd. gr. xx.

April 1st.—She has been very troublesome all night, and has required manual restraint. She is just as excited this morning, screaming at the top of her voice, throwing her arms about, and with difficulty detained in bed. Urine has been passed during the night into the bed, so could not be examined. Bowels have acted twice, and there is some œdema about the ankles. Two further doses of chloral hyd. gr. xx, were given during the day, and sulphonal, gr. xx, at night time.

April 2nd.—Passed a quieter night, but is as noisy as ever to-day; is removed to an asylum.

Patient remained in the asylum for four months, was then discharged recovered. An examination of the urine shewed albumen to have entirely disappeared, and there were no casts. Mentally, also, she is much better than at any time when seen previously.

CASE 8. *Uræmic Loss of Taste and Smell, occurring in the course of a case of Granular Contracted Kidney. Coma; Death.*—Robert A.——, aged 58, gentleman, complained of occasional loss of taste and smell lasting several hours, June 20th, 1891.

Previous History.—Patient has had fair health until the age of 45, when symptoms of gout appeared, the attacks of which have not been very severe or frequent. No history of syphilis, scarlatina, or other infectious disease. Present symptoms commenced six months ago, but latterly they have become more troublesome.

Condition on Examination.—He is a well nourished, slightly anæmic man; lately has lost flesh; no œdema; temp. 98·2 F.

Chest well formed; breath sounds, vocal fremitus and resonance normal. R. 22.

Heart's apex, fifth interspace inside nipple line, action

regular; heart sounds normal; slight accentuation of the aortic second sound. P 90, hard, incompressible; tongue slightly furred, indented at edges; bowels regular; no discomfort after food; appetite good; liver slightly enlarged; spleen normal.

Urine, 50 oz., sp. gr. 1010, acid, pale colored, slight precipitate. Urea, 1·75 per cent. Albumen, $\frac{1}{6}$. A few granular and hyaline casts; no blood or sugar; has been obliged to get up of late, two or three times a night, to pass water; pupils small, react to light and distance; atrophic patches in the retinæ of both eyes, but especially in the left; has not noticed any loss of vision; sensations of touch and pain, and reflexes normal; no headache. There is most complete loss of taste on the fore part of the tongue to acid, bitter, sweet, and saline substances; near root of tongue bitters can be detected; the loss of smell is absolute; states that symptoms usually last several hours, and are preceded by a slight tingling and numbness at the extremity of the tongue. Sensations of touch and pain in the tongue and nose are normal.

Treatment.—Ordered simple diet of milk and farinaceous foods, and forbidden more than one meat meal a day, and pastry or sweets. Stimulants restricted to four tablespoonfuls of whiskey a day with meals, and

℞				
	Quin. Sulph.	gr. ij	Magn. Sulph.	gr. xx
	Ac. Hydrobrom, dil.	q.s.	Syr. Aurant	ʒj
	Tr. Ferri perchl.	♏v	Aq. distil. ad.	ʒj

before each meal.

Purgation was secured by calomel gr. iv., and Hunyadi Janos water.

June 27th.—There is not much improvement; purgative acted well; following day he was better, but quickly relapsed into former state. Urine, 55 oz., sp. gr., 1012, acid; albumen, $\frac{1}{8}$; urea, 1·5 per cent.; casts as before; previous mixture stopped; bowels ordered to be kept relaxed; all red meat forbidden; naphthalin, gr. x, in cachet, to be taken one hour after each meal.

July 27th.—There has been considerable improvement since last note; loss of taste and smell still occasionally occurs, but at much greater intervals; latterly the naphthalin has made him sick four or five times. Urine, 53 oz., sp. gr. 1014, acid,

dark colored (naphthalin), albumen only a trace; urea, 1·75 oz.; no blood.

Naphthalin stopped for a few days until nausea had disappeared. Sodium sulphocarbolate, gr. x, substituted. The patient was not seen again until Oct. 3rd. For the last three or four weeks he has given up all treatment, although he is certain it was doing him good. He now complains of violent headache behind the eyes and in the frontal region, and loss of taste and smell are more pronounced than ever. Urine, 40 oz., sp. gr. 1016, acid; cloudy deposit; urea. 1·80; albumen, ¼; granular and hyaline casts; few blood cells; there is no œdema. Ordered diet as strict as before, and vapour baths thrice a week in his own house; calomel, gr. iv, and Hunyadi Janos whenever the bowels did not act freely; naphthalin, gr. x, to be recommended. Under this treatment headache soon disappeared and the albumen became less; advised to spend winter in the Canaries. On October 28th he was comparatively well; albumen merely a trace; urine, 50 oz.; no blood; few casts.

He returned home in April with some œdema of the feet and ankles. Says that for the last three or four weeks he has had constant occipital headache; swelling commenced on the steamer in consequence of a chill. He has been taking iodide of potassium for some time when away, but as it has had no effect upon the loss of taste and smell it was finally abandoned.

He is much thinner; temp. 98·6; heart sounds strong; apex beat outside nipple line; accentuation of the aortic second sound; pulse, 84; hard and incompressible, irregular. Lungs: signs of bronchitis throughout both lungs; dulness; loss of vocal fremitus and breath sounds over the right base extending to lower angle of scapula. Respiration 28.

Tongue coated; mouth dry: breath offensive; eye symptoms are much the same as when first seen.

Urine, 38 oz., sp. gr. 1018, smoky; deposits urates; albumen, ½ volume; urea, 1·9 per cent. blood; hyaline and granular casts

Ordered milk and farinaceous diet with chicken or fish; Pulvis Jalapæ Co, gr., xl, and Naphthalin, gr. x, in cachet, the latter to be taken as before; the right pleura was tapped and 40 ounces of serous fluid withdrawn; a hot-air bath given daily

for a week. Under this treatment œdema nearly disappeared, and he became a little better generally.

April 20th.—Has vomited several times; naphthalin stopped, and

℞ Pulv. Digit. gr. ss | Pulv. Scillæ gr. iss
Pil. Hydrarg. gr. iss |
Fiat pill, thrice daily, substituted.

April 25th.—The quantity of urine passed per diem since last note was 45 oz., 40 oz., 36 oz., 41 oz., 32 oz.; albumen varied from $\frac{1}{3}$ to $\frac{2}{3}$; urea from 1·2 to 2 per cent. There is much more œdema, which extends up the legs to the body; a slight return of fluid in right side of chest; resp. 25; temp. 97·6; Ordered vapour bath; kidneys cupped.

April 26th.—Skin perspired freely, but since bath has hardly passed any urine. He is very drowsy; snores loudly when asleep; lumbar region poulticed.

April 28th.—Has gradually been becoming comatosed; it is possible to awake him by shouting; he is very restless: stertorous breathing; high pitched; temp. 96·4.; pulse, 66; resp. 24; urine, 16 oz., sp. gr. 1024, acid, copious deposit, smoky; urea, 9 per cent.; albumen, $\frac{1}{8}$ volume.

℞ Calomel gr. iv | Ol. Croton ♏j
Placed on tongue.

Pilocarpine nitrate, gr. $\frac{1}{3}$, subcutaneously.

April 29th, 8 p.m.—He is evidently dying; deeply comatosed; urine passed and bowels moved, unconsciously. Eyes quite insensitive to light and pupils widely dilated; breathing stertorous; R 22; pulse, 60, irregular; skin acting freely. 6.30 a.m. he died.